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Original Communications

CONSERVATIVE SURGERY IN ENDOMETRIOSIS*

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CONSERVATIVE surgery in the treatment of endometriosis is the predilection of all gynecologists. That gynecologists vary somewhat on ideas of conservatism is to be expected. Dannreuther[1] feels that conservation of ovarian tissue in women over 35 years of age is of little importance, while Cashman[2] removes "the uterus and major lesions in the ovaries, if present," and attempts to "preserve all of the ovarian tissue possible." Graves[3] stated that removing ovaries hurts only neurotic women, yet he felt conservatism was in order when treating endometriosis. It finally becomes apparent that all gynecologists vary in their ideas of the importance of ovarian tissue, not to mention the childbearing capacity in a normal, healthy, well-adjusted woman.

Novak[4] states that each case must be individualized as to the extent of the lesion and the age of the patient. To us, conservative gynecologic surgery means the removal of the least possible tissue to obtain the desired result. Hence, every attempt is made to preserve ovarian function to the age of 45 years or beyond if the lesion permits, and in previously sterile women the preservation of childbearing capacity to the age of 40 years. A patient with endometriosis who has her family obviously minimizes the latter consideration.

Material and Problem

The material we offer consists of 80 consecutive cases encountered in the past six years. We have operated on 75 of these patients; we reoperated on four additional patients who had originally been operated upon elsewhere, and one patient operated upon elsewhere had recurring symptoms which we have been able to control without surgery.

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May we say here that this series does not include many patients we feel certain have endometriosis, although we have no pathologic proof. These we have been able to control so far without resorting to surgery. Our problem is, then: Is it possible in endometriosis to preserve a normal functioning, asymptomatic pelvis?

Technique and Operative Procedure

Fig. 1 is a cross section of a uterus and its adherent adnexa encountered in endometriosis. This familiar picture demonstrates the usual adhesive bed of ovarian heteroplasia. We have arbitrarily labeled ovarian lesions as "slight" when there is no appreciable enlargement, "moderate" where the ovary is about 5 to 6 cm. in diameter, and "advanced" where enlargement was beyond 7 to 8 centimeters.

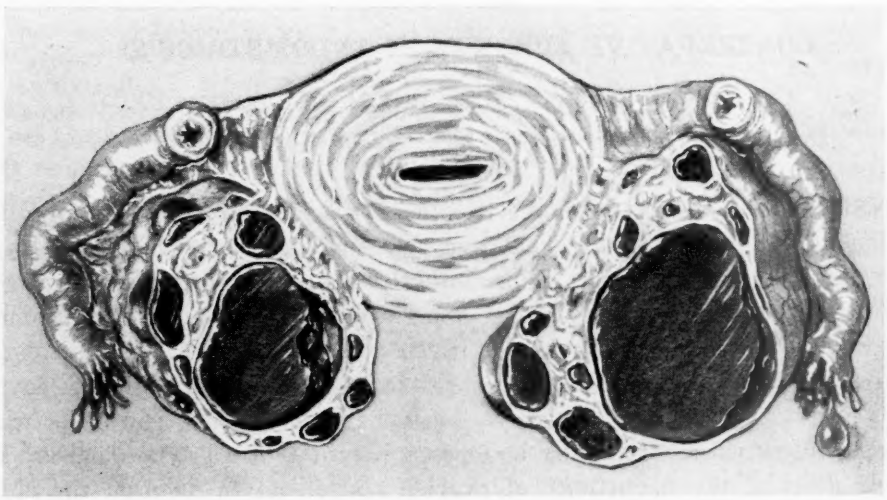

Fig. 1.

Fig. 2 illustrates our method of ovarian resection. The slight or early lesions were excised with repair of the ovary, usually by a small mattress suture of No. 00 chromic catgut on an atraumatic needle. Where we have moderate or advanced ovarian lesions, the ovary is delivered from its adhesive bed. Not infrequently rupture occurs during this procedure. The ovary is then opened by extending the point of rupture or, if no opening is present, by incision across the ovary directly opposite the hilus. The ovarian cyst is then opened like an oyster shell. All the affected tissue that can be seen is sharply dissected away and the ovary repaired with a continuous suture of No. 00 chromic catgut. Bleeding as a rule is not marked. However, if it does occur to any degree, small mattress sutures will control it.

In all cases, pathologic proof of diagnosis was obtained from resected or biopsied tissue. When removal of the uterus was deemed necessary, a panhysterectomy was done if the uterosacral ligaments and cul-de-sac involvement was not too marked. Appendectomies, if not previously done, were performed.

Retrodisplaced Uteri

In our series of 80 cases we have noted a rather high incidence of retrodisplacement (42.5 per cent). For this reason we have divided the cases into

two groups in order to note any difference in operative procedure. Further, if conservatism, by our definition, is possible, do the results justify the procedure?

The average age at operation of these 34 patients with endometriosis and retrodisplacement was 35.5 years. There were many pelvic complaints in this group; however, consultation was sought in the main because of varying grades of dysmenorrhea and dyspareunia with associated menorrhagia and/or metrorrhagia. One patient complained of backache, while two came to us for postmenopausal bleeding only.

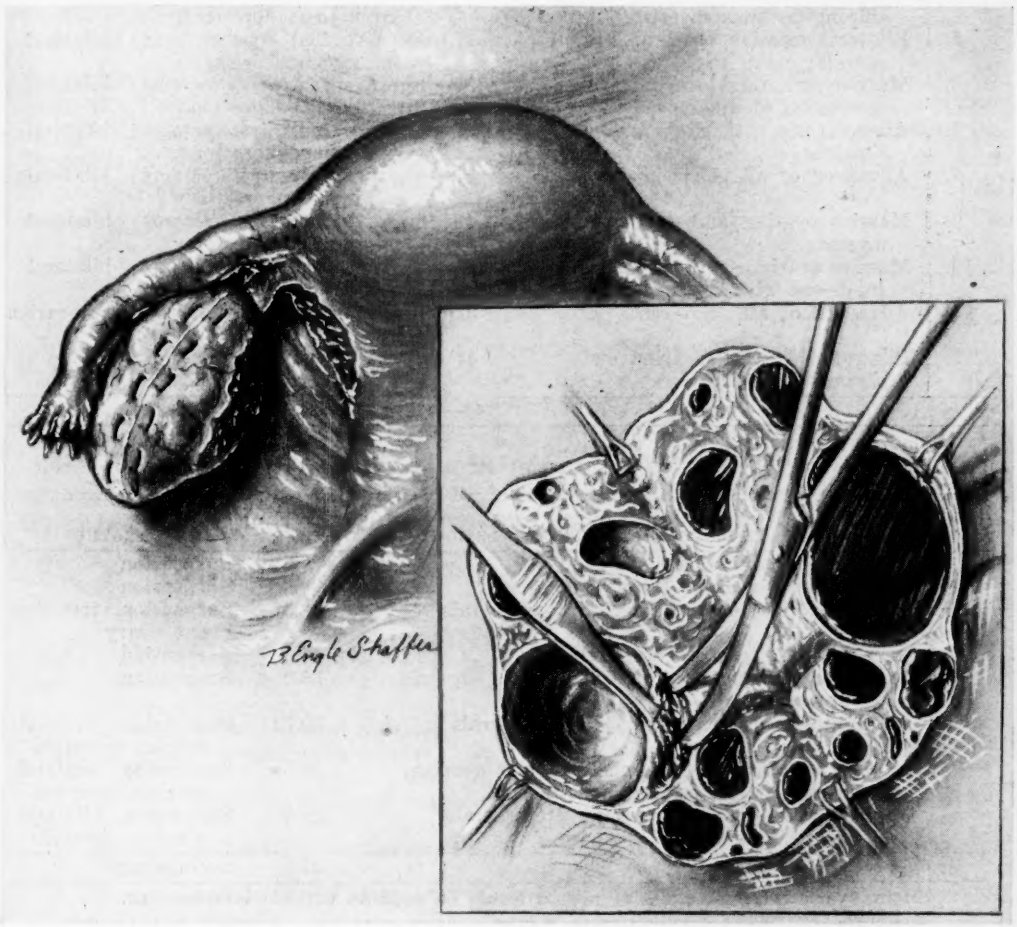

Fig. 2.

Table I (12 cases) summarizes the most severe cases in the retrodisplaced group. All of these patients had known retroversion for years. We consider the surgery to be radical in all. The ages ranged from 31 to 56 years, with an average age of 44 years. Unfortunately, three women were in the fourth decade of life, and in only one was any degree of conservatism possible, i.e., to leave ovarian tissue. A normal ovary was left in another patient 41 years of age. Both of these women are symptom free after three years, although endometriosis is palpable in the uterosacral ligaments at the moment. Two cases that were past the menopause at the time of operation (one with ovarian carcinoma) are free of symptoms and palpable pathology. The remaining eight have their

TABLE I. RETROVERSION AND ENDOMETRIOSIS

NO.	EXTENT AND LOCATION	AGE	SURGERY
1.	Advanced unilateral ovarian; utero-sacrals; cul-de-sac	41	Supravaginal hysterectomy; unilateral salpingo-oophorectomy
2.	Advanced bilateral ovarian; utero-sacrals; cul-de-sac	34	Supravaginal hysterectomy; unilateral salpingo-oophorectomy; resection one ovary
3.	Bilateral massive ovarian; cul-de-sac; uterosacrals; chronic salpingitis	31	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
4.	Bilateral massive ovarian; chronic salpingitis adenomyosis	40	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
5.	Bilateral massive ovarian; utero-sacrals; cul-de-sac	47	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
6.	Massive unilateral ovarian; adeno-carcinoma of other ovary	56	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
7.	Adenomyosis with slight evidence of ovarian	56	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
8.	Advanced of all pelvic viscera	47	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
9.	Massive ovarian and cul-de-sac with myomas	48	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
10.	Massive ovarian; uterosacrals and cul-de-sac with myomas	45	Supravaginal hysterectomy; bilateral salpingo-oophorectomy
11.	Advanced of all pelvic viscera	37	Unable to remove more than the ovarian growth
12.	Bilateral advanced ovarian and sigmoid with myomas	47	Panhysterectomy; bilateral salpingo-oophorectomy
		44—	average age

TABLE II. (TWENTY-TWO CASES) RETROVERSION AND ENDOMETRIOSIS

NO. OF CASES	PATHOLOGY AND EXTENT OF LESION	AVERAGE AGE	OPERATION
6	Uterosacral ligaments (slight)	30.3	Suspension
3	Unilateral slight ovarian, uterosacrals	30.3	Suspension
2	Unilateral moderate ovarian, uterosacrals	28.5	Suspension, resection one ovary
3	Bilateral slight ovarian, uterosacrals	31.3	Suspension
1	Bilateral slight ovarian, uterosacrals, sigmoid, appendix	33.0	Suspension
4	Bilateral moderate ovarian, uterosacrals	30.75	Suspension, bilateral ovarian resection
2	One advanced ovarian, one moderate ovarian, uterosacrals, broad ligament	35.0	Suspension, bilateral ovarian resection
1	Bilateral advanced ovarian; uterosacrals, broad ligament	29.0	Suspension, bilateral ovarian resection
		31.0—	average age

Slight ovarian (endometriosis) means lesion on capsule without enlargement.
Moderate ovarian (endometriosis) means ovaries enlarged to about 5 to 6 cm.
Advanced ovarian (endometriosis) means ovaries enlarged to or beyond 7 to 8 cm.

menopausal symptoms fairly well controlled. In this group, all of the patients had one or more children with the exception of the 37-year-old woman who was unmarried.

It will be noted that only one patient had a complete hysterectomy. It was not feasible to do a panhysterectomy in the remaining eleven women because of marked uterosacral and cul-de-sac involvement.

The remaining 22 cases of retroversion and endometriosis are shown in Table II. The average age was 31 years. Nine women demonstrated early or minimal lesions, yet enough to fix the corpus uteri in the cul-de-sac as firmly as the most advanced case in the group.

Infertility concerned seven patients, and four of these have conceived (two delivered, one aborted at eight weeks, and one is pregnant now). The most advanced case in the group (certainly the most likely candidate for an operative failure) conceived four years after surgery. Only one patient continued to have the same complaints we had hoped to relieve with operation. Medication afforded no relief. However, she conceived eight months after suspension and resection of one ovary. Another patient, two and one-half years after operation, has a recurrence of dyspareunia with an increase in cul-de-sac growth. She refused to attempt pregnancy. All the patients that conceived had no endometriosis palpable after the sixteenth week of pregnancy.

It is of interest to note that the uterosacral ligaments were involved in 91.3 per cent of the patients, while 72.7 per cent demonstrated ovarian lesions. In all cases the Baldy-Webster technique was used. There have been no recurrences of retrodisplacement, in spite of clearly palpable endometriosis in most instances. Progress of the disease is watched for mainly in the uterosacral ligaments, and in one instance we have been able to detect spread into the cul-de-sac or surrounding broad ligaments.

Uterus in Normal Position

There were 46 cases, or 57.5 per cent, of the series of 80 cases that had a normally placed uterus. We have divided these into groups of like pathology. Table III lists 13 cases of endometriosis with associated myoma uteri. It will be seen that the average age is 43 years, and again the need for conservatism was not great. In only one patient, aged 37 years, did we have the complaint of infertility along with the usual symptoms. This individual is now two years postoperative, has not conceived, but is symptom free. In all but this one case, the myomas precluded anything but hysterectomy. We were able to salvage

TABLE III. UTERUS ANTERIOR—ENDOMETRIOSIS AND MYOMATA

NO.	PATHOLOGY AND EXTENT OF LESION	AVERAGE AGE	OPERATION
1.	Bilateral moderate ovarian, round ligament, myomas	37	Myomectomy, ovarian resection
2.	Myomas, slight bilateral ovarian	40	Supravaginal hysterectomy
3.	Myomas, omental endometriosis	38	Supravaginal hysterectomy, resection omentum
4.	Myomas, moderate unilateral ovarian	40	Panhysterectomy, unilateral salpingo-oophorectomy
5.	Myomas, unilateral moderate ovarian	41	Supravaginal hysterectomy, unilateral salpingo-oophorectomy
6.	Myomas, unilateral moderate ovarian and uterosacrals	36	Supravaginal hysterectomy, unilateral salpingo-oophorectomy
7.	Myomas, bilateral advanced ovarian, cul-de-sac	44	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
8.	Myomas, bilateral moderate ovarian, cul-de-sac	48	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
9.	Myomas, bilateral advanced ovarian	41	Panhysterectomy, bilateral salpingo-oophorectomy
10.	Myomas, bilateral slight ovarian	55	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
11.	Myomas, bilateral moderate ovarian, tubal, sigmoid	45	Panhysterectomy, bilateral salpingo-oophorectomy
12.	Myomas, bilateral moderate ovarian	44	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
13.	Myomas, bilateral slight ovarian, cul-de-sac	55	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
		43—average age	

TABLE IV. UTERUS ANTERIOR—ENDOMETRIOSIS

NO.	PATHOLOGY AND EXTENT OF LESION	AGE	OPERATION
1.	Adenomyosis	44	Supravaginal hysterectomy
2.	Adenomyosis	42	Supravaginal hysterectomy
3.	Adenomyosis	40	Panhysterectomy
4.	Adenomyosis	30	Panhysterectomy
5.	Adenomyosis	40	Supravaginal hysterectomy
6.	Adenomyosis and myomas	45	Panhysterectomy
7.	Adenomyosis, myomas, broad ligament	43	Panhysterectomy
8.	Adenomyosis, unilateral moderate ovarian	49	Supravaginal hysterectomy, unilateral salpingo-oophorectomy
9.	Adenomyosis, advanced bilateral ovarian, uterosacrals, cul-de-sac	36	Supravaginal hysterectomy, unilateral salpingo-oophorectomy, resection one ovary
10.	Adenomyosis and complete prolapse	53	Vaginal hysterectomy
11.	Adenomyosis, myomas, cul-de-sac, unilateral advanced ovarian	49	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
12.	Adenomyosis, bilateral moderate ovarian	50	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
13.	Adenomyosis and myomas	51	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
14.	Adenomyosis, myomas, advanced ovarian, cul-de-sac	42	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
15.	Adenomyosis, myomas, bilateral advanced ovarian, cul-de-sac	40	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
		44—average age	

TABLE V. UTERUS ANTERIOR—ENDOMETRIOSIS

NO.	PATHOLOGY AND EXTENT OF LESION	AVERAGE AGE	OPERATION
1.	Bleeding endometriosis in cul-de-sac with 5 weeks' pregnancy	27	Exploratory only
2.	Implants on bladder and round ligament	29	Presacral neurectomy
3.	Bilateral advanced ovarian	30	Resection both ovaries
4.	Bilateral advanced ovarian	38	Resection both ovaries
5.	Bilateral moderate ovarian, uterosacrals	29	Resection both ovaries
6.	Bilateral advanced ovarian, unilateral chronic salpingitis	30	Unilateral salpingo-oophorectomy resection one ovary
7.	Unilateral moderate ovarian, uterosacrals, broad ligament, sigmoid	38	Unilateral salpingo-oophorectomy
8.	Bilateral advanced and moderate ovarian, uterosacrals, cul-de-sac	34	Unilateral salpingo-oophorectomy resection one ovary
9.	Unilateral moderate ovarian	39	Unilateral salpingo-oophorectomy
10.	Bilateral advanced ovarian, cul-de-sac	41	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
11.	Bilateral advanced ovarian, cul-de-sac	46	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
12.	Bilateral advanced ovarian, cul-de-sac, chronic salpingitis	40	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
13.	Bilateral advanced ovarian, tubal, sigmoid, cul-de-sac	42	Supravaginal hysterectomy, bilateral salpingo-oophorectomy
		36—average age	

ovarian tissue in situ in 46 per cent of the patients. None of these patients have pelvic complaints, although, again, endometriosis is palpable.

Table IV illustrates 15 cases of adenomyosis and adenomyosis with myomas and/or heteroplasia in the adnexa. The average age of this group was 44 years. All the operations must be considered radical in this group, although we were able to conserve all or part of the ovaries in 66 per cent of the patients. One patient was unmarried when we operated, the remainder of the group had two

or more children. The problem was one largely of trying to salvage ovarian tissue. Not considering four menopausal or postmenopausal patients, two women were surgically castrated between the ages of 40 and 42 years. In the latter two instances, conservatism seemed to us out of the question.

In Table V we have listed 11 cases of uncomplicated endometriosis, and two with additional findings. One interesting case was operated upon for ectopic pregnancy and was found to have bleeding endometrial tissue in the cul-de-sac (proved by biopsy). Another patient had minimal endometriosis of the bladder and round ligament with probable adenomyosis, in which case we locally excised the lesions and did a presacral neurectomy. Endometriosis was so extensive in 31 per cent of the patients (all 40 years old or over) that we could salvage no healthy ovarian tissue. It would seem in our attempt to group lesions according to extent that the treatment has varied greatly, i.e., ovarian resection in one advanced state and removal in another. Our explanation for this lies in the fact that one massive endometrial cyst when resected had some grossly healthy tissue, while another equally large growth seemed to lack even a small fragment of normal ovarian substance to be left behind.

Cases 3 through 8 could have had a complete ablation of the internal pelvic viscera according to usual standards of treatment. We are happy to note that these patients have none of their former complaints after a follow-up of one to six years. Thus far, in retrospect, we would not have changed the operative procedure in any of this group. Case 3 had a child 10 years of age when she was operated upon, and she was most desirous of another. She is symptom free so far, but has failed to conceive.

TABLE VI. FAILURES; OPERATED ELSEWHERE; FIVE CASES

PATHOLOGY AND EXTENT OF LESION	AVERAGE AGE	OPERATION OR TREATMENT
Advanced sigmoid (partial obstruction), cul-de-sac (9 years from previous operation)	26	Supravaginal hysterectomy and remaining tube and ovary
Advanced ovarian, cul-de-sac (4 years from previous operation)	45	Supravaginal hysterectomy and remaining tube and ovary
Adenomyosis, advanced ovarian and cul-de-sac (6 years from previous operation)	34	Supravaginal hysterectomy and remaining tube and ovary
Adenomyosis, moderate ovarian (5 years from previous operation)	32	Supravaginal hysterectomy and remaining tube and ovary
Moderate ovarian, cul-de-sac (5 years from previous operation)	34	Observation and control of dysmenorrhea with benzedrine and aspirin

In Table VI are listed five failures. These women had been operated upon conservatively elsewhere at the intervals stated in the table. Case 1 had a tragic history. Originally at 17 years of age a large endometrial cyst ruptured and the affected ovary was removed. She had no symptoms until 24 years of age when dysmenorrhea occurred with increasing severity. The following year the patient married and used contraception. We were consulted after six months of married life. At this time the patient not only had severe dysmenorrhea but crampy, intermittent pain in the left lower quadrant. Establishing a diagnosis of endometriosis was not difficult. The patient was advised to conceive if possible in the hope of slowing up the endometrial process and further hoping to have a family before a second operation was necessary. The patient could not conceive. Partial bowel obstruction soon put in its appearance and we were forced to operate at 26 years of age. The rectosigmoid and cul-de-sac involvement was so advanced that we had no other course but to remove the remaining tube, ovary, and uterus. The psychic trauma to this individual was marked.

Since the remaining four patients had children, they created not too great a problem. They all had one constant feature in history, i.e., the pain they were originally operated upon for was in no way improved by the first operation. None of them was the least bit interested in further conservative surgery but requested that everything responsible for their pain be removed. One 45-year-old patient in this group needing reoperation we classed as a failure since she was never free of pain following the first operation.

Comment

Nineteen patients, or 23.75 per cent, in the entire series were 45 years or older. Their treatment was radical although we salvaged ovaries in three instances. All of these patients have been well and we have no regrets at leaving the ovaries in three women over 45 years of age. Sixty-one, or 76.25 per cent, of the patients in the series were under 45 years of age. They constituted the main problem. Conservative surgery was impossible to any degree in 15 instances (24.5 per cent). Ovarian tissue was salvaged in whole or in part (by resection) in 14 patients (23 per cent). Childbearing capacity was retained in 32 cases (52.5 per cent). Follow-up examination revealed that for a period of one to six years all of these sixty-one cases have been free of complaints save two. One, at least, is temporarily asymptomatic with her pregnancy. A large share of the conservative treatment was possible through correction of a retrodisplaced uterus with its prolapsed adnexus.

We have been more than a little impressed with the incidence of retrodisplacement and endometriosis. It is well known that retrodisplacement receives scant attention in many quarters. This may be due to an overcorrection away from the days when it received entirely too much attention. Certainly an incidence of 42.5 per cent points to more than a casual relationship. Curtis[5] states, "In recent years we have learned that misplaced endometrial tissue is common with retrodisplacement." Sampson tells us in Sutton's[6] paper that, "The uterus is often but not necessarily always retrodisplaced." Watkins[7] injected contrast media into a retrodisplaced uterus without pressure and demonstrated it in the cul-de-sac. He points out the frequency of retrodisplacement and cul-de-sac endometriosis. However, the only figures we have found were those of Keene and Kimbrough,[8] finding an incidence of 13.5 per cent retrodisplacements while King[9] reports 21 per cent.

That there is a relationship in these two conditions cannot be denied. One wonders if the uterosacral ligaments may be a starting point in many of these cases since the minimal lesions were always there. Our feeling is that retrodisplacement with its mechanical interference with blood supply causing broad ligament varicosities, engorged cystic prolapsed ovaries, and passive congestion in the uterus, are accelerating factors in the metaplasia. For this reason we believe all women with retrodisplaced uteri should be observed at regular six-month intervals. Should they develop symptoms or demonstrate anything but a freely movable uterus a suspension is in order. In this way early lesions may be picked up while minimal, conservative surgery can be instituted and our salvage rate for the integrity of the internal pelvic viscera far higher. It would

seem thus far in this small series that when endometriosis and retrodisplacement are present suspension of the uterus retards the heteroplastic spread.

We believe resection of the ovaries in an attempt to uncover normal tissue is a worth-while procedure. Cattel and Swinton,[10] in a series of 43 cases, believe that complete ovarian involvement in endometriosis is not common and therefore emphasize conservatism. Failures in conservative surgery have been reported as high as 29 per cent by Pemberton[11] and as low as 7 per cent by Crile.[12] In the 46 cases under 45 years of age in which we saved the uterus, tubes, and ovaries or ovaries alone, we failed in one case to relieve pain, yet the patient conceived. In one other recurrent symptoms appeared at two and one-half years.

An assessment of operative success or failure can be made at the follow-up examination. As we have noted above, the outstanding feature of the failure of conservative surgery was unremitting pain.

Conclusions

1. There seems to be a close relationship between retrodisplacement and endometriosis.

2. The nonpathologic retrodisplaced uterus should be observed at regular intervals for signs of fixation indicating a surgical need for treatment of probable endometriosis.

3. We have found it possible to salvage ovarian tissue in situ in 23 per cent of women under 45 years of age.

4. Childbearing capacity was salvaged in an additional 52.5 per cent of women under 45 years of age.

5. For many years the diagnosis of endometriosis has been a carte blanche to surgeons for castration.

6. We feel that conservative surgery is definitely worth while and should be the major consideration when operating upon endometriosis.

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Discussion

DR. JOHN MONTGOMERY (Philadelphia).—I believe that we are all in accord with the fundamental principles enunciated in trying to be conservative in young women in the childbearing years with the extensive endometriosis which requires complete removal of the ovaries and uterus. It is easy enough to take out the uterus and, as a rule, we cure the patient,

but in some instances the patient is a very unhappy person for the rest of her life. In our clinic at Temple University that has been the rule and it has been surprising to me the number of instances in which conservatism can be practiced in certain patients who appeared hopeless on examination of the pelvis, and in whom the results have been very gratifying.

One of the problems mentioned, which I think is rather questionable, is that endometriosis is the result of retroversion. Certainly, endometriosis that perhaps begins in the ovaries and the cul-de-sac and, as it proceeds, sets up an inflammatory reaction may in many cases be the cause of the retroversion.

DR. WILLIAM P. HEALY (New York).—I would have been tempted to be less conservative than the essayist under similar conditions. For example, I doubt if I would try to conserve ovarian function in a woman 45 years of age with bilateral endometriosis. I would feel that we could probably satisfactorily control any annoying symptoms which the patient might have from total hysterectomy and castration by medical measures.

I definitely agree with Dr. Beecham in the extreme importance of recognizing fixed retroversion caused by endometriosis. Therefore, in a young woman who has some dysmenorrhea and probably is sterile and may have some dyspareunia, I believe there is an indication for surgery, not because of the retroversion, but because of her symptoms and the endometriosis, which must be present.

Now, why is the uterus retroverted? Not so much because the uterosacral ligaments are invaded and infiltrated by the glandular deposits, but because the rectum or rectosigmoid creeps up on the back of the uterus and pulls the uterus down into the cul-de-sac.

DR. FRED A. SIMMONS (Boston).—I can only cite Dr. Meigs' observations at the Massachusetts General Hospital and am curious to know if Dr. Beecham has the same findings. We find that the incidence of endometriosis is definitely greater in the private than in the ward patients. This may possibly be due to the restraint of normal pregnancy in the private group as compared with the ward group, and possibly to late marriage in the private group due to educational hazards toward early marriage and consequent reduced fertility in that group. The incidence of endometriosis in Dr. Meigs' private patients is around 40 per cent, and the ward incidence is 5 per cent. He is always looking for it and finds it in the uterosacral ligaments usually. In the ward patients we find it more commonly, if it is looked for, than we did ten or fifteen years ago.

DR. ROBERT A. KIMBROUGH (Philadelphia).—Some years ago Dr. Floyd Keene and I reported a series of 108 cases, in 48 of whom one or both ovaries were conserved. Within a period of five years only three patients required subsequent treatment. Of those in whom the possibility of pregnancy was conserved, 28 per cent had subsequent normal pregnancies.

I believe there is no question that conservative surgery is indicated in endometriosis for three very specific reasons: first, endometriosis is not a malignant condition; it is possibly in some few cases clinically, but never in itself histologically, malignant; in any benign condition conservative surgery is indicated. That is a broad general statement, but I think most of us will subscribe to it. In the second place the existence and spread of endometriosis is absolutely dependent upon ovarian function. When we operate on a patient with endometriosis and leave ovarian function, we are perfectly aware of the possibility that the endometriosis may continue to spread, and the present amount of endometriosis will persist and may continue to cause symptoms. That is the possibility, but since endometriosis is dependent upon ovarian function, and since irradiation is a very simple method of controlling ovarian function, it seems that conservative measures are indicated in the treatment of this condition. The third reason which warrants the use of conservative measures is the fact that this lesion is extremely slow in its development and spread; those patients who may later require further therapy may, therefore, enjoy the advantages of continued ovarian function for several additional years.

DR. JAMES R. MILLER (Hartford).—We see a great deal of this condition and I, like the others, bemoan the fact that it occurs in young women.

I think there are some other conservative measures that may be brought to bear. Occasionally, we encounter endometriosis in the rectovaginal septum and then it causes more alarm than it does when it is higher up. I think that direct x-ray, and even radium seeds applied locally, will control the lesion.

I would also like to mention the use of testosterone propionate or methyl testosterone by mouth as one of the conservative measures which may be tried. It is quite striking to see the reduction in size of the endometriotic lesions which will occur under testosterone propionate. That, of course, cannot be pushed too far, and caution must be used to keep the dosage well below 200 mg. per mouth.

DR. WILLIAM STUDDIFORD (New York).—I would like to ask Dr. Beecham the nature of the carcinoma that he found in association with endometriosis in the opposite ovary. The reason I ask that question is that we have now five cases in which there is a very strong indication that the ovarian carcinoma is actually adenocarcinoma arising on the basis of endometritic deposits in the ovary. In one of the cases the likelihood is almost beyond question.

I do not believe you can regard endometriosis in elderly women as something which is entirely beyond the pale of malignancy.

DR. INGLIS F. FROST (New York).—In the last two years I have been trying to see how much ovarian tissue could be resected and still maintain a positive secretory phase in the endometrial biopsy. We have had 25 cases at the Woman's Hospital in which we resected ovaries, leaving ovarian tissue not much larger than the head of a pin. When the secretory phase of the endometrium is maintained and the patients are ovulating they generally become pregnant easily, but it is very difficult for them to retain the pregnancy, and we feel that they must be given a great deal of supportive treatment in the way of progesterone.

DR. JOSHUA W. DAVIES (New York).—I feel that this is not a surgical condition, but that it is due to some endocrine dysfunction which results in the production of a great deal of pain in the pelvis, rendering it essential that we relieve patients so afflicted. Relief may be afforded by severing the adhesions in the pelvis, and thus holding the uterus anteriorly. I do not approve of removing the uterus or adnexa in these patients.

Dr. Beecham said that the uterosacral ligament is involved in many of these cases, chiefly on the left side. The uterosacral ligament is not a ligament alone; it is a very dense structure containing lymphatics, and when there is an inflammatory condition of the lymphatics there is production of scar tissue. If the uterus is involved with endometriosis, the denser peritoneum over the uterus is carried out to the lymphatics in the uterosacral ligament which run to and up the rectum. It is scar tissue in the uterosacral structure on the left side which draws the uterus against the cervix and rotates the uterus to the opposite side of the sacrum, to which the sigmoid is attached; this causes congestion in the pelvic circulation. Thus the uterus becomes fixed and the veins distended. If we fail to relieve these patients of their pain I believe surgery should be resorted to and in operating for retroversion, if it is possible to separate the sigmoid from the cervix and hold the uterus anteriorly, these patients may be temporarily relieved.

DR. E. EVERETT BUNZEL (New York).—There is one phase of the subject which was not touched upon and which was brought to my attention by a recent case. The patient was 40 years old with an ovarian mass on the right side and gave a history of having had a profuse, painful, long period. I opened the abdomen following a curettage, and found free blood in the abdominal cavity. Some of the blood was bright, while some had the character of the chocolate material found in Sampson's cysts. The cyst on the right side was not ruptured, but was adherent. After wiping away the blood in the pelvis we found several endometrial implants on the posterior aspect of the uterus, the posterior aspect of the broad ligament, and in the cul-de-sac. I wonder whether these implants are prone to bleed into the peritoneal cavity. At 40 years of age I did not take a conservative attitude, but removed the uterus and cervix together with the adnexa on both sides. The patient was married, but had never conceived.

By allowing one ovary to remain it would stimulate further activity and cause trouble from the endometrial implants, including bleeding into the peritoneal cavity.

DR. BEECHAM (Closing).—Dr. Montgomery stated that he believes endometriosis causes retrodisplacement. Six cases in our series presented minimal lesions on the left uterosacral ligament; these were so small it seems hard to believe that the endometriosis was an etiologic factor in the retrodisplacement.

In reply to Dr. Healy, we left ovaries in women 45 years of age and over only if they were normal grossly and the pathology was limited to the uterus. Both Dr. Miller and Dr. Healy mentioned the use of x-ray in the therapy of endometriosis. We have used it only for castration purposes, since it is very difficult to measure a subcastration dose in any given individual. We have seen permanent amenorrhea result from the so-called stimulating dose of x-ray to the ovaries for secondary amenorrhea and other endocrinopathies.

Dr. Simmons mentioned Dr. Meigs' work in reference to the frequency of endometriosis in private practice. The cases in this paper were all private patients, the disease having been seen but rarely in the wards at Temple University and Philadelphia General Hospitals. Meigs holds the view that late marriage and prolonged uninterrupted menses in any woman favors the development of endometriosis. This undoubtedly is one of the chief causes for the high incidence in private patients.

Dr. Kimbrough's series of cases have yielded a higher per cent of pregnancies in sterility patients than any other report we have seen. Dr. Kimbrough brought up a perplexing question; namely, that endometriosis depends on "ovarian function" for continual growth and development. In this we are all agreed, yet the ovaries function in pregnancy. In fact, the estrogen curve goes up as term approaches and endometriosis regresses to nonpalpable lesions.

Dr. Studdiford asked what kind of an ovarian carcinoma was encountered with endometriosis. It was an adenocarcinoma. Our impression was that the patient had bilateral endometrial cysts and one had undergone malignant change.

Dr. Frost has been able to demonstrate ovulation by endometrial biopsy after ovarian resection in cases of endometriosis. We have followed a number of the same type patients with daily rectal temperature readings for a short time following operation and have found all to have anovulatory bleeding for several months.

Our findings have been similar to Dr. Davies', that the left uterosacral ligament is the usual starting point for endometriosis.

Dr. Bunzel asked about bleeding of heteroplastic tissue in the free abdominal cavity. We have found it in the one reported case in the cul-de-sac, associated with early pregnancy.

THE TREATMENT OF PROLONGED LABOR WITH POSTERIOR PITUITARY EXTRACT*

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DURING the past fifteen years, with the advent of accurate methods of x-ray pelvimetry, a better understanding of the mechanism of labor has been observed in both the normal and abnormal obstetric pelvis. Accurate measurement and accurate classification of the abnormal obstetric pelvis has contributed much to a more intelligent conduct of labor.

The trend in obstetrics during the latter years has been to emphasize the architecture of the bony pelvis as the major factor in the prognosis of a given labor, with less regard being given to the other factors involved. This attitude is understandable when we consider how little is accurately known regarding the cause of the onset or the continuation of effective uterine contractions.

Helpful as these different techniques of x-ray mensuration may be in evaluating the pelvic architecture, we are always faced with the problem of the type of labor a given case may experience. It is this unknown factor which makes every obstetric case at least a potential problem. Certainly, it is a common experience to observe the successful completion of labor, even in the presence of rather marked pelvic contracture where labor is accompanied by effective uterine contractions. For contrast, severe degrees of prolonged labor may occur only in the presence of soft-tissue dystocia when associated with the ineffectual powers of labor.

In the dystocia group which results from pelvic contracture, the proper treatment can usually be ascertained after a few hours of a trial test of labor. Exceptions do, of course, occur in a small percentage of so-called "borderline cases." However, in the treatment of the dystocia group resulting primarily from ineffectual labor, the correct procedure to obtain a good result is often difficult to determine.

In the absence of any evidence of cephalopelvic disproportion, the common terms which have been used to describe this latter group are atoni uteri (primary or secondary), cervical dystocia, and delayed or prolonged labor. No term is entirely satisfactory. In any event, whatever term one desires to use in describing such cases, the problem remains the same; namely, the inability of the cervix to become completely dilated.

Unfortunately, watchful expectancy is not always associated with brilliant results in these cases of prolonged labor resulting from uterine inertia. It is common experience that fetal damage and maternal complications may produce disasters of as great a magnitude in these cases as in those patients who are subjected to prolonged tests of labor in the presence of cephalopelvic disproportion. As Douglas and Stander[1] have so aptly stated (in studying the effect of pro-

*Read before the Boston Obstetrical Society, November, 1945.

longed labor on the fetus), "prolonged labor per se exerts a deleterious effect on both the maternal and fetal organisms and the severity of this deleterious effect increased progressively with the duration of labor."

During the clinical course of these patients with prolonged labor, there may arrive a time when one must resort to an active policy. Manual dilatation of the cervix, the dilating bag, Dührssens' incisions, difficult forceps operations, and radical cesarean section have been recommended in the past. Certain of these methods are obsolete. All such methods are bound to carry an appreciable increase in the maternal and fetal mortality and morbidity rate.

The employment of x-ray pelvimetry does contribute a certain sense of security in the proper conduct of labor in these cases which are experiencing ineffectual labor. However, this can be deceptive if we should take the attitude that all patients who present little or no evidence of cephalopelvic disproportion will have their babies by the pelvic route if given a sufficient length of time to complete their labors. The obstetrician with this attitude must accept some increase in the infant stillbirth and neonatal death rate in proportion to the number of added hours or days of labor which are allowed to transpire. This group becomes even more important because we are concerned with good babies, at least at the onset of labor. So often this is not true in other complicated obstetrical conditions.

It follows, therefore, that in realizing the increased infant stillbirth and neonatal death rate which accompanies prolonged labor, we should employ every means at our command to decrease the number of such cases. Until we know the cause or causes of the onset of labor, any attempt to treat successfully such patients can be done only empirically, and is, therefore, subject to a certain percentage of failures.

During the past five years at the Boston Lying-in Hospital, we have used posterior pituitary extract routinely on all patients who revealed any evidence of inertia during the course of any patient's labor. It was felt that this was the most reasonable policy if we were to obtain a true picture of the merits and demerits of this drug. Although the drug had been used in this clinic in previous years for the treatment of uterine inertia, its routine use was not carried out in all cases of inertia. It was felt that enough experience had been gained in the use of x-ray pelvimetry (Thom's method) to insure against the giving of the drug to any patient with definite cephalopelvic disproportion. In addition, experience had been gained with the different types of extraperitoneal cesarean sections which could be resorted to if any untoward results occurred from the use of the drug or if it failed ot completely dilate the cervix.

The object in using the drug was as follows:

1. To attempt to decrease the number of cases of prolonged labor, by completing the dilatation of the cervix within the limits of the number of hours commonly associated with normal labor (thirteen to eighteen hours).

2. To treat cases of so-called prolonged labor with this drug in order to reduce the number of hours of the first and second stages of labor with its adverse effect on the fetus.

3. It was hoped that the necessity for difficult pelvic operations, such as midforceps with or without Dührssens' incisions, could be brought to a minimum in these cases of prolonged labor.

These are desirable aims if these conditions could be fulfilled without increasing the stillbirth and neonatal death rate, or producing latent cerebral damage to the infant or any deleterious effect on the mother. For it has been suggested that prolonged labor, per se, was not necessarily harmful in itself, but prolonged labor accompanied by a difficult forceps operation was a combination that was extremely lethal to the baby.

It was felt that the drug must be used in a sufficient number of patients in order to evaluate it properly. Such evaluation should include (in addition to the objective stated above):

1. What are the limitations of the drug.
2. What type of case was most likely to result in failure when the drug had been used. The factors which might have contributed to such failure should be ascertained.
3. If the drug had any merit, would it be possible to evolve a rational method whereby the drug could be safely placed into the armamentarium of the treatment of cases of so-called prolonged labor resulting from uterine inertia.

Material

This communication is concerned with reporting on 1,609 patients who had been given posterior pituitary extract during the first and second stages of their labors. These patients are divided into two series, 767 cases collected from private patients, and 842 cases from the clinic of the Boston Lying-in Hospital. The latter group is composed of cases treated during the past five years, while some of the records of the patients in the private series date back several years before x-ray pelvimetry and extraperitoneal cesarean section had become common obstetric techniques. This accounts for some of the differences in the private series in contrast to the clinic series, as for example, the type of operations necessary to complete delivery in each series.

Each of these series has been divided into two subgroups, the uncomplicated and the complicated. The element of time, i.e., the hours of labor which ensued, is the factor upon which these groups were classified. The number of hours of labor which must pass in order to make a diagnosis of prolonged labor varies in different clinics. We chose twenty hours of labor as the dividing line between the uncomplicated group and the complicated group. The diagnosis of prolonged labor was attached to the latter group. We realize that this is an arbitrary division. However, the normal length of primiparous labor is accepted as averaging from thirteen to eighteen hours. We extended the time to twenty hours in order not to include any cases in the prolonged labor group (complicated) who were not actually troublesome cases.

Many of the cases in both the complicated and the uncomplicated groups were diagnosed as patients with prolonged labor. Individual perusal of the patient's records did not substantiate such a diagnosis in many of the cases. Although the patients were experiencing at times irregular and painful contractions, the patient was not in true labor. For this report, the onset of true labor was defined and so recorded as beginning only when the uterine contractions were of such quality that definite changes could be recorded regarding either effacement, but more particularly still, some degree of dilatation of the

cervix. Desultory uterine contractions which might be continual for hours or even days were present in many of these patients in both groups, but if the above changes on the cervix could not be ascertained, the patient was considered to be in false labor and was so treated.

Results

In Table I is recorded the age of the patients. The general age group follows a general trend both in the private and clinic series. Most of the cases were primiparous women; two-thirds were under 30 years of age.

TABLE I. AGE

	20 TO 29 YEARS	30 TO 39 YEARS	40 YEARS	TOTAL CASES
Private series, uncomplicated	442 61.2%	265 26.9%	10 1.50%	717
Boston Lying-in series, uncomplicated	460 72.5%	161 25.3%	15 2.30%	636
Private series, complicated	34 68.0%	16 32.0%	–	50
Boston Lying-in series, complicated	168 81.6%	36 17.5%	2 0.97%	206
Total cases	1,104	478	27	1,609

Parity.—In Table II it is shown that age and parity go hand in hand. About two-thirds of the entire series are primiparous women. There is one difference, however, to be observed between the private and the clinic series. There are many more primiparous patients treated in the clinic series than in the private series.

TABLE II. PARITY

	i	ii TO iii	iv	TOTAL CASES
Private series, uncomplicated	390 54.4%	294 41.00%	33 4.50%	717
Boston Lying-in series, uncomplicated	452 71.0%	143 22.50%	41 6.40%	636
Private series, prolonged labor	44 88.0%	6 12.00%	– –	50
Boston Lying-in series, prolonged labor	199 96.6%	2 0.97%	5 2.43%	206
Total cases	1,085	445	79	1,609

In Table III is recorded the parity of the complicated group occurring in the clinic series. It can readily be seen that there were very few multiparous women who came to so-called prolonged labor. These exceptions can be readily explained. This is a small but important number of patients who will compose a group who may be justifiably classified as "dangerous multiparas." These cases composed about 3 per cent of this complicated clinic group. This group deserves further comment. Suffice it to say that large babies, accompanied by some degree of pelvic contracture, were present in these multiparous patients and uterine inertia was of secondary importance.

The station of the head at the onset of labor is listed in Table IV. Only about one-fifth of the patients entered labor with the presenting part unengaged. It could not be established whether the patient who started in labor with an unengaged head was more likely to present evidence of prolonged labor. The station of the head at the onset of labor was not a factor in the production of prolonged labor.

TABLE III. BOSTON LYING-IN HOSPITAL (CLINIC SERIES, COMPLICATED)

Parity:	i	ii to iii	iv
Cases:	199	*2	*5
Per Cent:	96.60	0.97	2.43

*(1) Para iv, large baby (8 lb., 10 oz.). Platypelloid pelvis.
(2) Para xiii, large baby (9 lb., 9 oz.). Platypelloid pelvis.
(3) Para iv, large baby (9 lb.). Platypelloid pelvis with android fore-pelvis.
(4) Para v, large baby (10 lb., 1 oz.). Gynecoid pelvis with android tendency.
(5) Para ii, large baby (9 lb., 1 oz.). Breech.
(6) Para iv, plastic operation between pregnancies.
(7) Para ii, no cause for dystocia.

TABLE IV. STATION OF HEAD AT ONSET OF LABOR

	HIGH	MID	LOW	TOTAL
Private series, uncomplicated	149	251	317	717
	20.9%	35.0%	44.70%	
Boston Lying-in series, uncomplicated	148	393	95	636
	23.3%	62.0%	14.80%	
Private series, complicated	14	26	10	50
	28.0%	52.0%	20.00%	
Boston Lying-in series, complicated	76	128	2	206
	37.9%	61.4%	0.97%	
Total cases	387	798	424	1,609

TABLE V. LENGTH OF FIRST STAGE OF LABOR

	4 TO 8 HOURS	9 TO 12 HOURS	13 TO 16 HOURS	17 TO 20 HOURS	TOTAL
Private series	409	185	78	45	717
	57.0%	25.8%	10.9%	6.3%	
Boston Lying-in Hospital series	388	173	74	1	636
	61.0%	27.2%	11.6%		
Total cases	797	358	152	46	1,353

In Table V the length of the first stage of labor is shown in the uncomplicated group in both series. Five-sixths of the patients had a first stage of labor of less than twelve hours, while half the patients delivered in less than eight hours. An overall average of the first stage of labor would fall between six and eight hours, which is about the average for a multiparous labor. With a high percentage of the primiparous women in the series, the overall length of the first stage of labor was, therefore, decidedly shorter than the usual standard taken for the average length of labor in primiparous patients. How many of these patients would have experienced prolonged labor if pituitary extract had not be given is problematical.

TABLE VI. LENGTH OF FIRST STAGE OF LABOR, COMPLICATED GROUP

	20 TO 29 HOURS	30 TO 39 HOURS	40 TO 49 HOURS	50 HOURS	TOTAL
Private series	44	4	2	–	50
	88.0%	8.0%	4.0%		
Boston Lying-in series series	128	54	15	9	206
	61.6%	27.2%	7.3%	3.9%	
Total cases	172	58	17	9	256

In Table VI is shown the length of the first stage of labor in cases of prolonged labor. In the complicated group, nearly 90 per cent of the cases, the completed first stage of labor was short of thirty hours' duration. The labors were somewhat more prolonged in the clinic patients, but only 11 per cent of this

series had a first stage labor of forty hours or longer. It should be emphasized, however, that many of these patients were in so-called desultory labor for perhaps as long as twenty-four to seventy-two hours before the actual true labor began. During that time no change was noted in the cervix, and consequently the patient was not considered to be in labor. Consideration of this factor may account in part for the low incidence of prolonged labor in this series in contrast to the experience of other clinics.

The length of the second stage of labor in the uncomplicated group (Table VII) revealed a sharp contrast between the private and the clinic series. The clinic series was subjected to many more hours of second stage labor. The reasons for this marked difference could be explained by the following factors: (1) The individual attention which would be given to the private patient where the responsibility is dependent upon one person would necessarily make its effect felt in shortening the second stage of labor. (2) The increased amount of pituitary extract which was used in the private series would necessarily shorten the second stage of labor (Tables X and XI). (3) In the clinic series a longer second stage of labor was believed justified in the hope that the patient would come to an easy low forceps operation. The drug was given specifically to further the descent of the fetal head in an attempt to reduce the need for a midforceps delivery. This would appear to be reasonable when we consider that the fetal mortality in the two series was approximately equal.

From the evidence presented here, we do not need to fear a prolonged second stage labor as long as the patient is making progress. The only fear in a prolonged second stage labor appears to be when progress has ceased. This is particularly true when this arrest of progress occurs with the presenting part on the perineal floor. It is generally agreed that if progress has ceased when this has occurred, delivery should be carried out with dispatch. To emphasize this, the babies that were lost in the clinic series (uncomplicated group, Table XV) occurred in a prolonged second stage labor associated with just such an arrest.

TABLE VII. LENGTH OF SECOND STAGE OF LABOR, UNCOMPLICATED GROUP

	1 HOUR	2 HOURS	3 TO 4 HOURS	5 TO 6 HOURS	7 HOURS	TOTAL
Private series	688 96.0%	29 4.0%	–	–	–	717
Boston Lying-in Hospital series	225 35.4%	173 27.2%	197 31.0%	32 5.0%	9 1.4%	636
Total cases	913	202	197	32	9	1,353

TABLE VIII. LENGTH OF SECOND STAGE OF LABOR, COMPLICATED GROUP

	1 HOUR	2 HOURS	3 TO 4 HOURS	5 TO 6 HOURS	7 HOURS	TOTAL
Private series	47 94.0%	3 6.0%	–	–	–	50
Boston Lying-in series	31 18.1%	76 44.7%	38 22.7%	19 11.1%	6 3.5%	170*
Total cases	78	79	38	19	6	220

*Certain patients who were given pituitrin eventually had to be delivered by extraperitoneal sections or Dührssen's incision; hence, no second stage of labor.

In Table VIII is given the length of the second stage of labor in the complicated group. Again it will be seen that the clinic series was subjected to a much longer second stage labor, no doubt for reasons already mentioned.

In Table IX is listed the types of deliveries. It will be noted that there is a much higher incidence of midforceps operations in the private series. This

TABLE IX. TYPE OF DELIVERY

	NORMAL	LOW FORCEPS	MIDFORCEPS	HIGH FORCEPS	VERSION	CRANIOTOMY	BREECH	CESAREAN	TWINS	TOTAL
Private series, uncomplicated	384 52.9%	277 38.1%	23 3.1%	9 1.2%	11 1.5%	– –	18 2.5%	4 2.5%	–9 1.2%	726
Boston Lying-in series, uncomplicated	204 32.1%	421 66.2%	6 1.0%	– –	3 0.5%	– –	5 1.0%	– –	–3 0.5%	639
Private series, complicated	12 23.5%	25 49.0%	7 13.9%	2 3.9%	3 5.9%	– –	2 3.9%	– –	–1 0.5%	51
Boston Lying-in series, complicated	18 8.6%	138 66.0%	16 7.65%	– –	1 0.5%	2 0.95%	7 3.35%	27* 12.9%	–3 1.5%	209
Total cases	618	861	52	11	18	2	32	31	–16	1,625

*Extraperitoneal (Waters) or exclusion type (Smith).

is offset, however, by an extremely low incidence of cesarean section. In contrast to this, there were no high forceps operations in the clinic series, while the midforceps incidence was very low. However, there were twenty-seven cases of extraperitoneal or exclusion types of cesarean section which gave a much higher incidence of cesarean section in the clinic series than in the private series. These differences can be readily explained when we consider that many of the private patients were delivered before the advent of extraperitoneal cesarean section or the general use of x-ray pelvimetry. It was considered advisable to do the occasional high forceps delivery where labor was prolonged and associated with possible intrauterine infection rather than subject the patient to a Porro cesarean section, which was then in order during the particular years in which many of these patients were delivered.

The use of the extraperitoneal or peritoneal exclusion cesarean section is a necessary method of delivery in certain cases of prolonged labor. It is a general policy of the clinic to use the extraperitoneal type where cesarean section is necessary for infected cases, or even in supposedly clean cases if labor is prolonged beyond twelve hours after the onset. This is particularly true if the fetal membranes have been ruptured prior to the beginning of labor.

There were 55 such operations performed in the past five years in the clinic of the Boston Lying-in Hospital. Four-fifths were of the Waters type and the remainder were the Smith exclusion type. There were two maternal deaths. One was due to shock and hemorrhage, and the other was an anesthetic death. There were two fetal deaths. It was interesting to note that these two fetal deaths (both due to asphyxia), occurred in babies whose mothers were allowed to continue in labor when progress had ceased for over twelve hours prior to section.

The indications for section could be divided roughly into thirds; namely, borderline cephalopelvic disproportion, questionable cephalopelvic disproportion with cervical dystocia, and finally, cervical dystocia per se. Uterine inertia was common to all, and it was felt in all of these patients that if labor was of good character, pelvic delivery was possible. Conservative obstetrics demand adequate tests of labor in these patients. Twenty-seven of these patients experienced prolonged labors. They were given posterior pituitary extract with poor effect during their labors in the hopes of overcoming the uterine inertia and associated cervical dystocia.

In Table X is detailed the maximum dose of posterior pituitary extract which was administered at any one time. Considerable differences in the dosage exists between the private and clinic series. It will be seen that much larger single doses of the drug were used in the private series in contrast to the clinic

TABLE X. PITUITRIN, MAXIMUM DOSE

MINIMS	I	II	III	IV	V	TOTAL CASES
Private series, uncomplicated	213 29.8%	243 33.9%	145 20.2%	42 5.8%	74 10.3%	717
Boston Lying-in Hospital series, uncomplicated	592 93.1%	42 6.6%	2 –	– –	– –	636
Private series, complicated	9 18%	24 48%	10 20%	2 4%	5 10%	50
Boston Lying-in Hospital series, complicated	139 67.4%	45 21.9%	19 9.2%	3 1.5%	–	206
Total cases	953	354	176	47	79	1,609

TABLE XI. PITUITRIN, TOTAL DOSAGE

MINIMS	1 TO 4	5 TO 9	10 TO 14	15	TOTAL CASES
Private series, uncomplicated	475 66.3%	173 24.1%	43 6.0%	26 3.6%	717
Boston Lying-in Hospital series, uncomplicated	605 95.1%	28 4.4%	3 0.5%	– –	636
Private series, complicated	30 60%	12 24%	7 14%	1 2%	50
Boston Lying-in Hospital series, complicated	116 56.3%	56 27.2%	19 9.2%	15 7.3%	206
Total cases	1226	269	72	42	1,609

series. This suggests that in the use of this drug the dosage should be increased until the patient has effective uterine contractions. We are justified in suggesting this when we consider the end results in the two series. It seems probable that our results in the clinic series (complicated group) might have been improved had we used the drug in increasing doses until a definite therapeutic effect was demonstrated.

Table XI reveals the total amount of drug used in a given labor. Again it will be seen that the total dosage used in the private series was much greater in most instances than in the clinic series. This again suggests the possibility that the drug could have been used in larger doses in order to obtain the most effective physiologic result.

TABLE XII. DEGREE OF CERVICAL DILATATION WHEN PITUITRIN WAS FIRST GIVEN

DILATATION	¼	½	¾	FULLY DILATED	TOTAL CASES
Private series, uncomplicated	58 8.1%	441 61.5%	46 6.4%	172 23.7%	717
Boston Lying-in Hospital series, uncomplicated	38 5.97%	32 5.03%	70 11%	496 78%	636
Private series, complicated	3 6.0%	38 76.0%	– –	9 18%	50
Boston Lying-in Hospital series, complicated	2 0.97%	27 13.10%	72 34.95%	105 50.98%	206
Total cases	101	538	188	782	1,609

Table XII reveals the degree of cervical dilatation existing at the time that pituitrin was first administered during the first stage of labor. Here again it is seen that the drug was administered in the private series much earlier in labor than in the clinic patients. This may indicate that as soon as progress in labor

had ceased in the private patients, the drug was immediately given, while in the clinic series this was not necessarily true.

We have been impressed by the lack of accurate knowledge of the degree of the dilatation of the cervix in the complicated group of the clinic series when dilatation was slow or had entirely ceased. A great variation occurred in the recorded degree of dilatation of the cervix as determined by different examiners, even when the examinations were done simultaneously.

We feel that the routine use of the rectal examination can be very inaccurate in attempting to determine the degree of cervical dilation in patients who are making unsatisfactory progress. Pelvic examinations should be resorted to when there is any question of the degree of progress or lack of progress that these patients are making. It is only in this manner that accurate evaluation in changes of the cervix can be made, and a more intelligent understanding of the problem can be ascertained.

Furthermore, we have been impressed by the degree of dilatation of the cervix which occurs in patients who fail eventually to dilate their cervices completely. With rare exception, cervical dilatation ceased in these cases when the cervix was between one-half and three-fourths dilated. So many times the cervix was thought to be nearly fully dilated by rectal examination, when on vaginal examination the above condition was found to exist.

It will be noted from this chart that the drug was administered in many of the private patients when the cervix was only half dilated. The criticism that severe injuries to the birth canal or that the drug is ineffectual when administered this early in labor is not substantiated by the results of this study.

Fetal Mortality.—(Stillbirth and neonatal deaths.) We have corrected the fetal mortality by eliminating premature infants (babies under 5 pounds), infants with congenital defects, erythroblastosis, or babies in whom the fetal heart was absent at the onset of labor. We have eliminated all the babies who were lost due to accidents of labor, such as prolapse of the cord. We have also eliminated babies who were lost because of antepartum bleeding due to premature separation of the normally implanted placenta and placenta previa, and babies who were born by breech extraction. There were six cases that were eliminated because of mid or outlet pelvic contracture, with associated difficult forceps, but not associated with prolonged labor. Two cases of prolonged labor which were not excessive in length and who showed no lack of progress, and, therefore, did not receive any posterior pituitary extract, were eliminated.

Table XIII represents babies who died for an unascribable cause in the clinic during the past five years. This represents the large group of patients

TABLE XIII. UNASCRIBABLE CAUSES OF FETAL DEATH. NO POSTERIOR PITUITARY EXTRACT DURING LABOR

	ASPHYXIA	INTRACRANIAL HEMORRHAGE	AUTOPSIES	NORMAL DELIVERY	OUTLET FORCEPS	DELIVERY CASES	PER CENT MORTALITY	TOTAL
Stillborn	20	0	15	18	12	11,506	0.17	
Neonatal deaths	13	6	11	13	6	11,506	0.17	0.33

Eliminate:
(1) Premature and immature infants.
(2) Congenital defects, erythroblastosis, absent fetal heart on admission.
(3) Accidents of labor, prolapsed cord, and premature separation of placenta, etc.
(4) Breech extraction.
(5) Prolonged labor or difficult forceps, eight cases.
2 cases: Prolonged labor, asphyxia.
6 cases: Mid and outlet contracture, intracranial hemorrhage.

who come to the hospital at full term with no complications, either obstetric or medical, in which the baby was normally developed and living at the onset of labor. Furthermore, the course of the mothers during labor was entirely normal in respect to both character and length of labor. The mothers were delivered either normally or by outlet forceps. No pituitary extract was given to any of these patients during the first and second stages of their labor. For unascribable reasons, the baby died in utero during labor or in the neonatal period. As is shown in the chart, comparatively few died from intracranial hemorrhage; the majority died of intrauterine asphyxia. During this five-year period, there were 39 such cases associated with 11,507 normal or outlet forceps deliveries, giving a total percentage mortality of 0.33 per cent. This represents in reality the irreducible fetal mortality and should form a base line in any study involving fetal mortality. Philosophically, it could be looked upon as the inherent or initial risk of being born. This fact emphasizes that even in a normal labor the baby undergoes some degree of intrauterine asphyxia.

Furthermore, had any of the mothers of these babies been given even the smallest amount of pituitary extract during their labors, it would, no doubt, have been considered that the fetal death had been due to the injudicious use of this drug.

TABLE XIV. FETAL MORTALITY, PRIVATE CASES, UNCOMPLICATED

TOTAL CASES: 717			CORRECTED FETAL MORTALITY
Erythroblastosis	2		
Congenital anomalies	4		
Baby dead on admission	4		
Intrauterine asphyxia		3	
Intracranial hemorrhage		2	
Total	10	5	0.69%

TABLE XV. BOSTON LYING-IN HOSPITAL, UNCOMPLICATED FETAL MORTALITY

TOTAL CASES: 636			CORRECTED FETAL MORTALITY
Fetal heart absent	4		
Prolapsed cord	3		
Von Gierke's disease	1		
Hemorrhagic disease	2		
Congenital anomalies	2		
Intrauterine asphyxia		2	
Intracranial hemorrhage		2	
Total	12	4*	0.63%

*All cases in second stage labor for four hours each. Three cases had only 1 minim of pituitrin at full dilatation. One case had only 2 minims and total of minims 4 with full dilatation of cervix.

In Tables XIV and XV are listed the causes of fetal death in the private and clinic series in the uncomplicated groups. It can be observed that the fetal mortality was extremely low in those babies who theoretically should have been born alive. Again, intrauterine asphyxia was more outstanding than the problem of intracranial hemorrhage as a cause of fetal death.

Table XVI is the computation of the fetal mortality in all the series and groups in this study. Intrauterine asphyxia occurred four times as often as intracranial hemorrhage. This was even more impressive as the cause of death in those cases who were subjected to prolonged labor.

Of most importance is the high fetal mortality rate in the clinic series who were subjected to prolonged labor (complicated group, 11.65 per cent). This is about the fetal mortality rate that is generally reported in other studies

TABLE XVI. CORRECTED STILLBIRTH AND NEONATAL MORTALITY

	NUMBER OF DEATHS	CAUSE OF DEATH		PER CENT MORTALITY
		PRIMARY ASPHYXIA	INTRACRANIAL HEMORRHAGE	
Unascribable group	39	33	6	0.33
Private series, uncomplicated	5	3	2	0.69
Boston Lying-in series, uncomplicated	4	2	2	0.63
Private series, complicated	2	2	0	4.00
Boston Lying-in series, complicated	24*	20	4	11.65

*Five deaths were associated with 17 cases of Dührssen's incisions.

of the effect of prolonged labor on the infant irrespective of the type of treatment employed. It is this group which truly represents the effect of prolonged labor on the infant. We have failed to treat properly such cases. It is well if we are to try to improve the treatment of these cases to evaluate carefully the factors which have contributed to such failures.

TABLE XVII. FACTORS IN THE STILLBIRTH AND NEONATAL MORTALITY. BOSTON LYING-IN COMPLICATED GROUP

24 cases		(3) Prolonged labor without lack of progress		(5) Reasons for lack of progress	
(1) Abnormal pelves	7	(4) Prolonged labor with lack of progress		a. contracted outlet	3
(2) Prolonged labor		a. 10 to 20 hrs.	18	b. inertia	19
a. 20 to 40 hrs.	17	20 hrs.	4		
41 to 60 hrs.	3				
60 hrs.	4				

In Table XVII is listed some of the factors which have contributed to such a fetal mortality in the complicated clinic series. Borderline pelves were perhaps a contributing factor in seven cases. Prolonged labor, per se, was, of course, the outstanding factor. Of most interest in this respect are the seven babies who were lost in patients who were subjected to labors of more than forty hours' duration. When we consider that only 26 cases in the entire clinic series were subjected to over forty hours of labor, this leaves us with a fetal mortality in the particular group of 29 per cent.

However, there are other factors which contribute not only to this fetal mortality, but also to the initial fetal mortality of 11.65 per cent. One of the most outstanding is the lack of progress prior to delivery which had occurred in those labors where the babies were lost. Not only do we have the factor of prolonged labor, but in addition we have what we believe is a most important factor, namely, the many hours of labor that were allowed to elapse even in the absence of any increase in the dilatation of the cervix. In other words, we not only subjected the patient to many hours of labor, in these cases where babies were lost, but we have subjected them to many hours of some sort of labor after progress had ceased. In 22 of the 24 babies lost, 18 were subjected to from ten to twenty hours of additional labor without progress, and four other babies were subjected to twenty hours or more without progress. This would suggest that this is one of the most important factors contributing to the high fetal mortality in this complicated group of cases. Even if a difficult pelvic delivery were anticipated in these cases, "watchful waiting" was not necessarily the correct procedure.

It will be further seen that the causative factor in this lack of progress was attributed to uterine inertia. Although pituitrin extract was used, one is

reminded that the amount of the drug was perhaps not used in doses which were sufficient to overcome this inertia. We would emphasize, however, that this group of cases illustrates the fact that the uterus may be or can become refractory to the drug.

In Table XVIII are listed the weights of babies in both series. It was thought that perhaps there was an increase in the average weight of babies which might have been a contributing factor in this type of dystocia. The over-all average was not significant when compared with a group of normal controls. However, there was a slight increase in the number of very large babies in the complicated group, and in those patients who were subjected to extraperitoneal cesarean sections.

TABLE XVIII. INFANTS' WEIGHTS

WEIGHT IN POUNDS	5 TO 6	6 TO 7	7 TO 8	8 TO 9	9	NOT RECORDED	TWINS	TOTAL
Private series, uncomplicated	36 6.0%	129 21.1%	247 40.5%	144 23.6%	54 8.8%	116	9	726
Boston Lying-in series, uncomplicated	37 5.6%	135 21.2%	231 36.2%	184 29.0%	52 8.1%		3	639
Private series, complicated	3	13	16	4	3	12	1	51
Boston Lying-in series, complicated	17 8.0%	38 18%	78 37.3%	56 27.3%	20 9.5%		3	209
Total cases	93	315	572	388	129	128	16	1,625
Normal control series	7.3%	21.8%	40.8%	24.3%	6.3%			

Discussion

The problem of prolonged labor in the absence of cephalopelvic disproportion still remains one of the major problems in obstetrics. This is, no doubt, due primarily to the fact that we have no method of treating these cases which is entirely satisfactory. So little is known about the action of the uterus during labor. Little or nothing is known about why certain uterine contractions are effective and others fail to perform their normal function.

Measurements can be made of the types and frequency of uterine contractions, but of how much practical clinical value these methods may be for devising ways and means of treatment for these disturbing cases is debatable.[2] Until we know the physiologic cause of labor, we still must grope our way along in an attempt to treat this most stubborn of all obstetric conditions.

Two attitudes toward the treatment of these cases have been suggested. One is built around the idea that the patient will eventually deliver herself if subjected to enough hours of labor. The treatment is dependent primarily on general supportive measures. This involves the resting of the patient from time to time, usually with opiates, and keeping the patient in positive fluid balance by the use of much parenteral fluids. This is certainly in order in every case where the patient is not in true labor. Stimulation of labor during this time is truly contraindicated.

The second attitude follows the belief that once the patient has started in true labor (by this we mean that the cervix is beginning to dilate), progress should be definite and sustained until that patient is successfully delivered. To

suggest the use of posterior pituitary extract as the means of producing sustained progress in the labor of such patients is looked upon by many as a very questionable procedure. Those who would condemn the drug cannot see any rationale for its use. They condemn it because they believe that when it is used in the first and second stages of labor, great trauma is produced to the birth canal as well as possible severe intracranial damage to the infant.

The literature in expression of these opinions is voluminous. Reports of rupture of the uterus, birth trauma to the infant, are always reported as being due to the use of this drug, and for the most part many of the other factors are ignored. Many of these cases so reported of severe trauma to the birth canal do not make it clear whether the problem of cephalopelvic disproportion was considered. In any event, to condemn a drug purely because it is not used properly is an unscientific approach.

We believe that the drug, posterior pituitary extract, can be administered safely during labor. From this report we believe that we have demonstrated that it is possible to give posterior pituitary extract in the first and second stages of labor without undue harm to either mother or baby. We believe that it has, like many drugs in medicine, its demerits as well as its merits. We have not been so impressed by its dangers as by its limitations. These limitations are due primarily to the fact that in certain cases of prolonged labor, a desired physiologic effect is not always obtained with its use.

Certainly we have decreased the incidence of prolonged labor, and in doing so, we have not produced any deleterious effect on mother or baby. Knowing the relatively high fetal mortality which accompanies prolonged labor, we feel that if it is possible to decrease the incidence of this syndrome that this very definitely justifies the use of the drug. The incidence of prolonged labor varies in different clinics, but in this clinic for the past five years when the drug has been used in inertia cases, prolonged labor has occurred in only about 2 per cent or even less in all cases delivered. This is two to five times less frequent than the usual incidence quoted for this complication. Midforceps operations have been done only 56 times during this five-year period, which is an incidence of 0.5 per cent. This operation is being done four to eight times less often than the incidence is usually reported. The use of Dührssen's incisions have been limited. In those cases where this operation was necessary, the fetal mortality was high (30 per cent). This is not to condemn this procedure. The results with this operation might have been improved had we resorted to it earlier in the course of a given labor after progress had failed to occur after a reasonable time.

We feel that our mistakes in using posterior pituitary extract have occurred because we have failed to appreciate fully that the drug will not produce progress in all patients. Furthermore, we have failed to realize that the drug could be used in larger initial and total doses in order to insure sustained progress. This is emphasized by the increased dosage used in the private series in contrast to the clinic series.

The failures which have occurred appear to follow a very definite pattern in these cases of prolonged labor. First, progress usually ceases when the cervix

becomes one-half to three-quarters dilated. Posterior pituitary extract will be given without effect. The patient still makes little or no progress, and many valuable hours elapse in which the baby in the meantime is suffering from an increasing degree of intrauterine asphyxia. After a period of twelve to twenty or even forty hours has elapsed with no further progress, the patient is finally delivered by either Dührssen's incisions or extraperitoneal cesarean depending upon the degree of dilatation of the cervix, estimated size of the infant, and finally, evaluation of the pelvis, particularly in regard to the capacity of the midpelvis and the pelvic outlet. It should be emphasized that this is the usual sequence of events when the so-called conservative policy is pursued, and where posterior pituitary extract is not used. The fetal mortality associated with such a course in labor (however treated) raises the problem of whether we can better our results by a more rational policy of treatment.

Before we suggest such a policy of treatment, there is one group which deserves special comment. It will be seen in Table III that in the complicated clinic group the number of multiparous patients who were given posterior pituitary extract was extremely small. Criticism of giving these patients pituitary extract is valid, for it seems most reasonable that a patient who has successfully dilated the cervix in a previous labor should be able to do it again. However, there are those that believe that the entity of cervical dystocia does not exist, but that the problem is one of inertia. This is difficult to reconcile because it appears that once the cervix becomes completely dilated or is incised (Dührssen's incisions), dilatation of the cervix in subsequent labors is never a problem if there is no cephalopelvic disproportion. If inertia plays the dominant role in these, why do we not seem to observe it in subsequent labors?

To emphasize this point of view, it will be noted that only one out of seven cases of prolonged labor occurring in the multiparous patients was caused by uterine inertia per se (Table III). Unrecognized cephalopelvic disproportion was at least in part a contributing factor in their dystocia. In other words, these cases composed a small group of the occasional but extremely important group of so-called "dangerous multiparas." These are individuals who had previous pelvic deliveries with living children, the babies usually being small or, at best, average in size. During the pregnancy in question the pelvis had not been properly evaluated. The babies were much larger than any they had previously delivered. This factor, combined with borderline or a definitely abnormal pelvis, resulted in a dystocia on the basis of cephalopelvic disproportion. In other words, inertia associated with cervical dystocia is a syndrome restricted with rare exception to primiparous women. This suggests that any multipara who is in true labor and does not deliver herself before twenty hours after the onset of labor should be regarded with great suspicion. Other factors, such as contracted pelvis, abnormal presentation, or extremely large infants, may be the cause for the dystocia. Failure to recognize and properly treat such a group may well be the source of most of the cases of spontaneous rupture of the uterus. Stimulation of labor in the multiparous patient who is experiencing prolonged labor should be done with great caution, and only after careful observation regarding the above factors.

On the other hand, it seems reasonable that a more rational method of attack might be suggested for these primiparous patients undergoing prolonged labor. If one is willing to concede that progress is imperative in all cases in which the patient has committed herself to dilatation of the cervix (true labor), then we are confronted with the problem of how best to carry out such a program. If one can see any merit in the use of posterior pituitary extract, then it would seem possible that we should be able to suggest a policy whereby it could be put to its most effective use.

In these patients who are experiencing prolonged labor in the absence of cephalopelvic disproportion, it is essential that degrees of progress should be measured carefully. As has been stated, rectal examination ofttimes is inaccurate, and frequently it is much better to resort to a sterile pelvic examination to ascertain the exact degree of dilatation of the cervix. This is particularly true if one is convinced that progress is not being made. It is only in this manner that one can date accurately the time in which progress has ceased. From this study we feel that lack of progress over twelve hours is not only detrimental, but may be lethal to the infant. We believe that the twelve hours which will elapse after progress has ceased is the most important time of the patient's labor.

This is the time which should be utilized for the stimulation of labor. If one desires to use posterior pituitary extract for such stimulation (and this seems to be the only effective means which one can employ), then a definite method of treatment can be outlined.

We shall administer pituitary extract for at least two reasons. First, to give the drug in the hopes of producing progress, as denoted by further dilatation of the cervix. Second, to attempt to ascertain whether we can expect progress. By this is meant that if the uterus is refractory to the drug, is it not reasonable to say that the uterus is refractory to further progress of labor. Assuming this to be true we can then start with the premise that we are giving the drug in increasing doses in order to produce progress, or, having given a reasonably large dose without effective progress, we can then turn to other means of terminating the labor. In this manner we have demonstrated in a comparatively short period of time that further progress will not take place. In this way we not only save the mother many hours of nagging uterine contractions which are ineffectual, but we have perhaps saved the fetus from irreversible damage. It is suggested, therefore, that we will give this drug in cases of prolonged labor as close to the time that progress has ceased as possible. The dosage should start with minims one and increase minims one every thirty to forty-five minutes until effective uterine contractions are produced. This dosage should increase, if necessary, up to a four-minim dose at a single dose. The size of the dose, of course, is regulated by the effect. Effective uterine contractions may ensue with the initial dose, and, in like manner, no effect may be obtained by a larger dose. However, if no effective uterine contractions or progress has been obtained after one to four minim doses have been used (which will cover a period of from two

to three hours) it seems reasonable then to discontinue the drug and turn to other means of completing labor. Procrastination from that point on will only add further hours of labor with its accompanying increased fetal mortality.

Conclusions

1. Prolonged labor, dependent on uterine inertia and associated with cervical dystocia, is a syndrome occurring with rare exception only in primiparous women.

2. Such exceptions are not due to cervical dystocia per se, but many occur in the "dangerous multiparas" with definite or borderline cephalopelvic disproportion.

3. We have administered posterior pituitary extract to 1,609 patients who exhibited any degree of uterine inertia during their labor.

4. The initial dose of this drug was usually one minim. The dosage was increased up to four minims at a single dose in an attempt to stimulate uterine contractions. Usually cervical dilation would ensue with the smaller doses.

5. The total dose in a given labor was usually one to four minims, but doses from five to nine, ten to fifteen, and even fifteen minims plus were administered during a single labor.

6. With the use of this drug there have been no cases of ruptured uterus or extensive birth canal trauma in this series.

7. The incidence of prolonged labor has been reduced to the low figure of 2 per cent in the clinic patients.

8. The need for midforceps operations in the clinic patients was reduced to 0.5 per cent. The need for Dührssens' incisions was small.

9. Some degree of intrauterine asphyxia accompanies normal labor. In this series it was 0.33 per cent.

10. Prolonged labor contributes materially to an increased fetal mortality. This is particularly true if more than forty hours in length.

11. Fetal mortality in the clinic patients with prolonged labor was 11.65 per cent, a figure which usually accompanies such cases. Intrauterine asphyxia was the most frequent cause of fetal death.

12. An attempt to evaluate the factors which contributed to this fetal mortality have been analyzed.

13. A policy in handling cases of prolonged labor with special regard to the use of posterior pituitary extract has been presented.

The author wishes to thank Dr. Frederick C. Irving for the use of his personal records which represent the patients reported as the "private series."

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THE ELECTRICAL POTENTIALS OF THE HUMAN UTERUS IN LABOR*

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IT MAY seem odd that an anatomist should discover electricity, but when Luigi Galvani touched frog muscle with a charged metal plate and found that it twitched, a broad and profitable field of medical investigation was opened. It remained for Volta, Oersted, and Einthoven[1] to develop means of measuring the force of this phenomenon, but once the galvanometer was in common use, its application for recording the electrical potentials accompanying activity of the heart, striated muscle, and brain was merely a matter of time.

Electro-investigation of the smooth muscle containing organs, however, has lagged far behind because of at least three factors: the structures are relatively inaccessible, the voltages emitted are small, and the interpretation of the findings has been exceedingly difficult.

One of the earliest investigators to study the uterine electrical phenomena was Theilhaber,[2] who, in 1910, thought he had found a significant difference in the action of the string galvanometer in women whose uteri and ovaries were intact as differentiated from those after the menopause or following hysterectomy. Metal electrodes were used, one on the cervix and the other in the rectum. Veit,[3] a few years later, was unable to detect uterine currents by applying one metal electrode to the arm and another to the leg, but obtained large deflections from the cardiac cycle. Blumenfeldt and Dahlman,[4] attempting to correlate changes in potential from the uterine horns with the mechanical action of the uterus as determined by a balloon in the cavity, were able to obtain definite deflections of the galvanometer string coincident with the uterine contraction (mechanically produced), but stressed the fact that in some instances voltages varied without corresponding muscle contraction.

More than ten years passed before further attempts were made to clarify the problem. In 1928, Greene[5] found that the galvanometer deflection which accompanied muscle contraction had a high frequency and that the amplitude of the deflection increased as the contraction gained strength, and Hasama,[6] in 1930, using Zn-ZnCl electrodes directly on the rabbit uterus, was able with the string galvanometer to record deflections of over a millivolt with a frequency of 10 to 15 cycles per second. Bode,[7] in 1931, using the string galvanometer and metal electrodes which were standard for electrocardiography at that time, placed the electrodes on the abdomen at the level of the umbilicus, and during labor noted a deflection of the string during the contractions of labor with a degeneration of the deflection as the uterine tone decreased. This seems to be the only report of an attempt to record changes in electrical potential from the human uterus in labor.

*The opinions expressed here are those of the authors and do not necessarily reflect those of the Navy Department.

Vozza[8] found correlation between the changes in potential and the contraction wave in experimental animals, but he too found some deflections of the string which were not associated with obvious muscle contraction. In 1935, Falk and Nahon[9] described action currents taken from the uterus of the human by an intrauterine silver electrode, and found that these currents could be definitely correlated with the ovarian cycle. Jacobson and co-workers extended these findings.[10]

Up until this time the electrical activity of the organ had been determined by the string galvanometer of Einthoven or a modification. The need for the study of the direct current components of smooth muscle activity has long been recognized, and Burr and associates[11] emphasized the requirements of any direct current amplifying system in the study of smooth muscle potentials, and described the changes occurring in uterine activity in association with the ovarian cycle.[12]

A great deal of work on smooth muscle has been done by Bozler,[13-15] who has shown that the contractions of the smooth muscles of laboratory animals are accompanied by bursts of impulses which are biphasic and carry a potential of one to two millivolts.

Our interest in the problem of the electrical phenomena associated with contractions of uterine muscle arose when planning a study of the physiology and pathology of labor. It seemed reasonable to suppose that the functional and conduction defects of the heart in severe myocardial damage, abnormalities of the bundle of His, and others, might well have a uterine counterpart. With this in mind, a systematic trial of some of the more likely methods of amplifying and recording electrical currents was instituted, and the findings are presented.

Materials and Methods

Evidence of electrical activity taken from the uteri of laboratory animals has demonstrated high frequency changes in potential associated with muscle contraction, and published curves also show a slow and maintained deflection of the string from the base line as do studies of the human uterus. It was therefore felt that investigation with both alternating and direct current amplifiers and recorders would be necessary in order to clarify the part played by each component.

The first alternating current amplifier and recorder used in the investigation was the portable electrocardiograph. This instrument is essentially a vacuum tube amplifier which responds uniformly to frequencies of one to 50 cycles. The recording is made on rapidly moving photographic film by an oscillograph driven by a resistance-condenser coupled amplifier. A one millivolt input signal causes a deflection of 10 mm. of the light beam. German silver metal plates, 4 by 5 cm., and electrode paste to reduce polarization and improve contact with the skin, were used. One electrode was placed just lateral to the umbilicus and the other (indifferent electrode) on the upper portion of the thigh.

The portable electroencephalograph* was the other alternating current amplification method used. It is a five-stage resistance capacity coupled ampli-

*This instrument was furnished by Dr. Paul Traugott of the Electro-Physical Laboratories, 25 West 18th Street, New York, New York.

fier which, with filters on, records accurately within the range of one to 35 cycles per second and gives a deflection of one centimeter with an input signal of ten microvolts. The deflections are recorded by magnetically driven inking pens upon a uniformly moving paper roll. The electrodes used were solder pellets 7 to 8 mm. in diameter, coated with electrode jelly and made adherent with collodion and adhesive tape. One electrode was placed lateral to the umbilicus and the indifferent one placed on the upper portion of the left thigh. The instrument was suitably grounded.

In order to determine electrical activity which might occur at a frequency of less than one cycle per second, it was found necessary to search for a suitable direct current amplifier and recorder. The vagaries of this type of amplification are well known, and only after much difficulty was an instrument obtained. This amplifier is a vacuum tube direct current amplifier with moderate sensitivity, high input impedance, with enough output to drive a pen-writing instrument.† The recorder is a sensitive magnetically-driven pen which records on a calibrated paper at a rate of 3 inches per minute.‡ This combination of instruments produces a deviation of the writing pen of one-half inch for an input signal of one and one-half millivolts. Drift is not negligible but is at a minimum for this type of amplification, and the pen of the recorder responds sluggishly to any input frequency of more than one cycle per second. Electrodes are fluid (.85 per cent sodium chloride in distilled water) to prevent polarization, and contacts are platinum. The area of skin contact was encircled with collodion to prevent changes in area with stretching of the abdominal wall. The platinum lead wires to the electrodes were attached to the amplifier through shielded copper wires, and the instrument was suitably grounded.

Patients at term in all stages of labor and prelabor were utilized in this investigation. All were volunteers, were cooperative, and were impressed with the necessity of restriction of voluntary motion.

Results

Group One.—Obtained by the portable electrocardiograph. Six patients. The records obtained by the portable electrocardiograph, using metal electrodes, one placed on each side of the umbilicus, are represented by the tracings in Fig. 1.

Tracing *A* represents the effect of the uterus in labor but in the absence of a contraction. The fetal and maternal electrocardiograms are seen and voluntary muscle effects are in evidence.

Tracing *B* was taken from the same uterus during a contraction and shows an initial upward deflection of the galvanometer. The patient was moderately comfortable during this contraction; she made every effort to cooperate in avoiding voluntary motion and none was obvious to the observers.

Tracing *C* shows the action of the galvanometer during a contraction in which the patient was under ethylene anesthesia, carried to a sufficient degree to obliterate all voluntary motion, but still sufficiently light to allow the uterus to contract spontaneously.

†This is a Type 715-A direct current amplifier manufactured by General Radio Company, Cambridge, Massachusetts.

‡This is the Esterline Angus supersensitive recorder in which one milliampere gives a full scale deflection.

These tracings are fairly characteristic of what is observed by this type of amplification and recording. Tracing *B* seems the only one of note if a departure of the galvanometer from the normal pattern is sought; its configuration is not unlike that reported by Bode.[7] No high frequency components are noted here that are not ascribable to the maternal or fetal cardiac current, but only a slow departure from the base line, denoting a change in potential of low frequency. However, since no large deflections of this type were noted under a general anesthetic, it would be reasonable to suppose that it was an artifact due to voluntary muscle contraction, despite the fact that the patient produced no obvious undue motion.

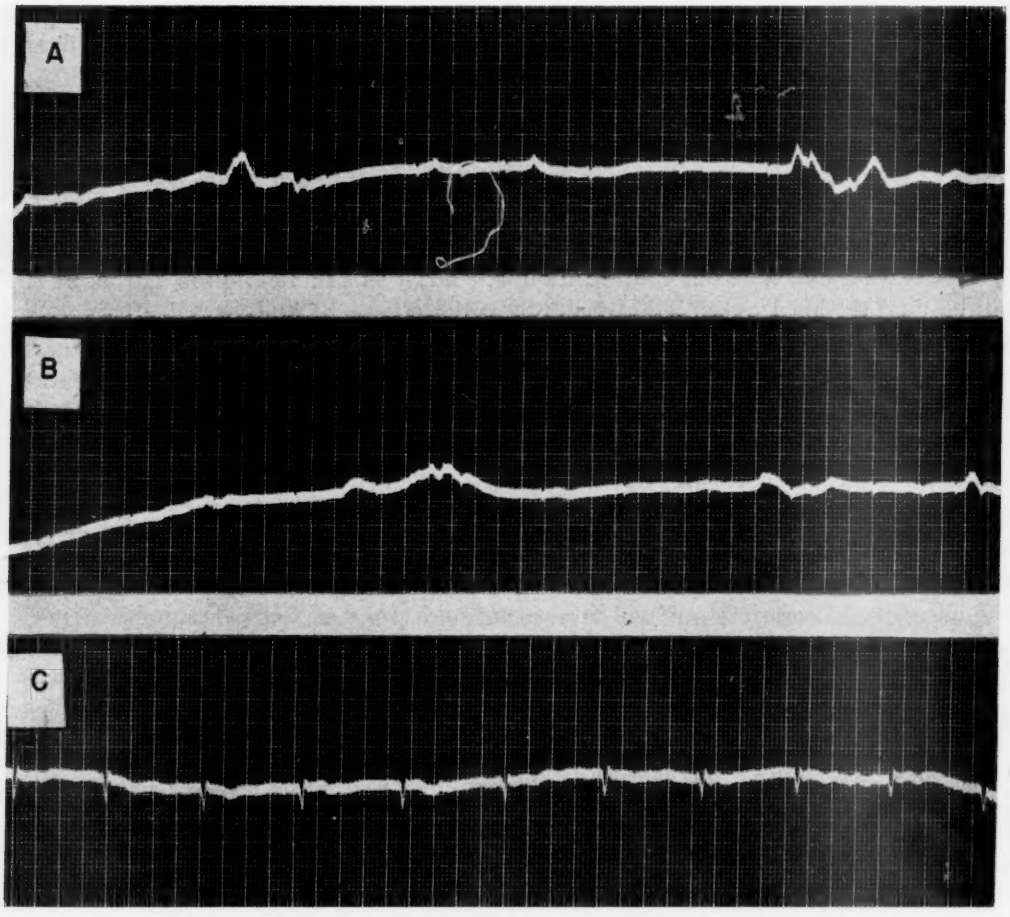

Fig. 1.—Tracings taken by the portable electrocardiograph.

A. **This tracing was taken during labor but while the uterus was relaxed. There was no analgesia.**

B. **During this period the uterus was contracting strongly. There was no analgesia.**

C. **The uterus during this tracing was contracting strongly. The patient was lightly anesthetized by ethylene and oxygen and all voluntary muscular action was reduced to a minimum.**

Group Two.—Obtained by the electroencephalograph. One patient.

In order to be more certain that high frequency changes in potential were not being missed through a lack of sensitivity of the recording mechanism, an electroencephalograph was used on one patient. Fig. 2 shows the result of this attempt.

Tracing *A* represents the activity recorded from the uterus of a patient actively in labor but with no contraction at the time of this tracing. The maternal and fetal electrocardiograms are again in evidence, and a minimal amount of voluntary muscular activity.

Tracings *B* and *C* were taken during a moderately severe contraction during which there was a minimal amount of voluntary muscular activity on the part of the patient.

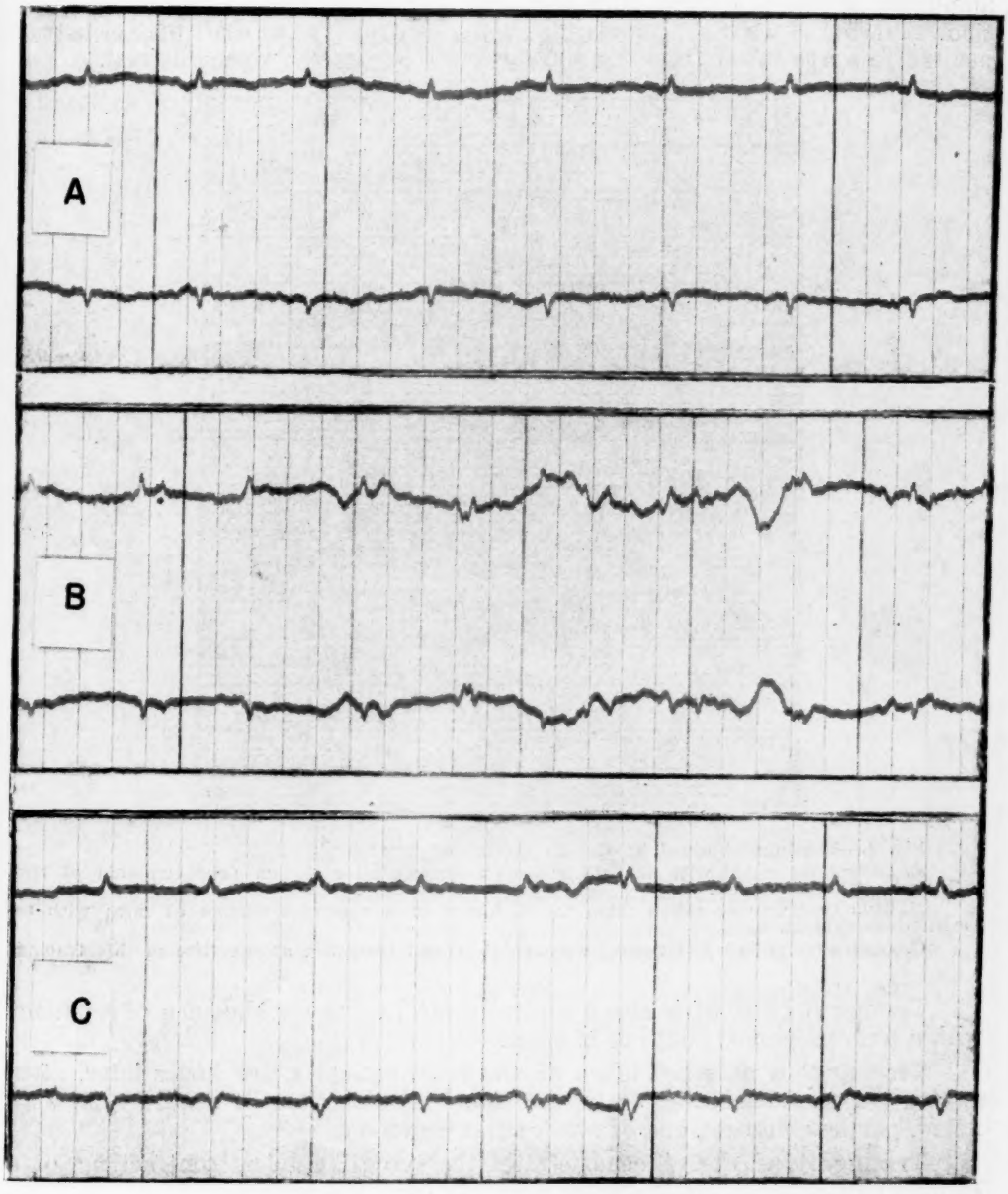

Fig. 2.—Tracings taken by the portable electroencephalograph.
A. This tracing was taken in labor while the uterus was relaxed between contractions.
B. This tracing represents the uterus actively contracting.
C. This tracing was also taken during an active contraction.

Here as in the records made by the electrocardiograph there is no clear cut evidence of high frequency components accompanying the muscular activity of the uterus.

Group Three.—Obtained by direct current amplification. Ten patients.

Figs. 3, 4, 5, 6, and 7 show tracings obtained on patients by the direct current amplification method described.

Because of the excessive "drift" which occurs in most direct current amplifiers, frequent control runs are made throughout the period of observation. Tracing *A* (Fig. 3) represents such a control for the drift of the instrument. This was taken from the abdomen of a nongravid woman at rest.

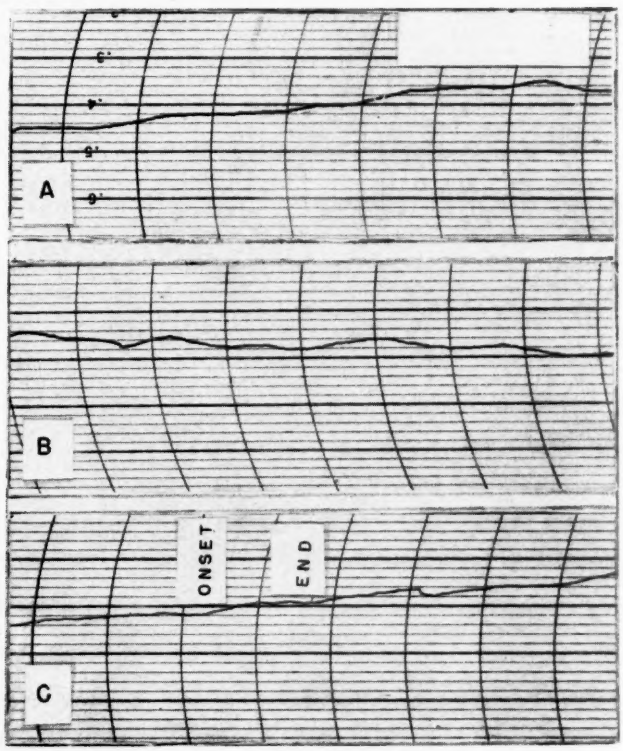

Fig. 3.—Tracings obtained by the direct current amplifier.

A. Deflections noted with the electrodes on the control abdomen (nonpregnant) at rest with no anesthesia or pain.

B. This tracing was taken from the abdomen of a pregnant woman at term with no contractions evident.

C. Contractions had just begun, were painless and irregular, at the time of this tracing.

Tracing *B* (Fig. 3) is also a control record, using the abdomen of a patient with a term pregnancy, but not in labor.

Tracing *C* is a record taken on the same patient a few hours later, after rupture of the membranes to induce labor. Contractions of a mild type were noted, painless, fleeting, and of nondescript character.

Tracing *A* of Fig. 4 demonstrates the typical painless contractions of a definite nature which are known as Braxton-Hicks contractions.

Tracing *B* (Fig. 4) was taken after the patient was in moderately severe labor. This patient was extremely cooperative, had no sedation at this point, and was as well "relaxed" as is reasonable under this type of labor.

Tracing *C* (Fig. 4) was taken after the patient had been lightly anesthetized by ethylene-oxygen anesthesia. There was good relaxation, and voluntary muscle ability was abolished, but the uterus was still contracting.

When caudal anesthesia was utilized, several very obvious differences were noted in the tracings. The greatest was the absence of vast changes in the overall potential obtained. In these patients the deflection caused by a contraction was a departure from a relatively straight line, while in the patients feeling pain during the contractions, the deflections of the contraction were larger but were accompanied by such huge changes in skin potential that many times they were dwarfed.

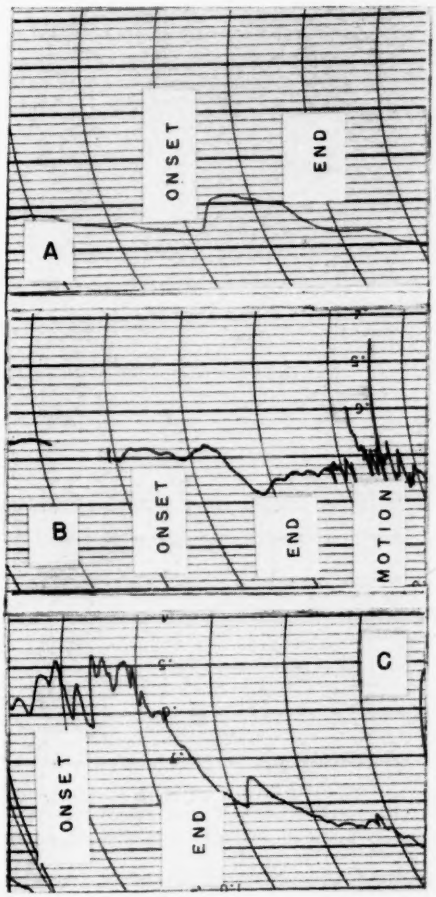

Fig. 4.—Tracings obtained by the direct current amplifier under no analgesia.

A. Contractions here are still painless but regular, and the uterus is moderately firm to palpation.

B. The contractions represented by this tracing accompanied early labor. The uterus was moderately tense.

C. This patient was in the second stage of labor and contractions were of good quality. The record was taken under light ethylene anesthesia.

Fig. 5 demonstrates tracings taken under caudal anesthesia. Tracing *A* was taken immediately after the inception of the caudal anesthetic when the contractions were mild, irregular, and had little effect in producing cervical dilatation.

Tracing *B* (Fig. 5) demonstrates the change in potential produced by the same uterus during hard contractions of such a nature that the cervix attained full dilatation in one-half hour from an initial five-centimeter stage.

Tracing *C* (Fig. 5) was taken on a patient who had had fourteen hours of severe "driving" labor while overcoming a moderate disproportion between the head and pelvis. The rapidity of onset of these contractions and their long duration is noteworthy.

Fig. 6 is designed to show the great difference in the tracings obtained under caudal anesthesia and those obtained without analgesia. It should be emphasized that morphine, scopolamine, the barbiturates, and rectal ether were all considered but were discounted because the patient who is moderately or heavily sedated is unable to cooperate, and enough of these drugs to produce loss of all motion would be unsafe.

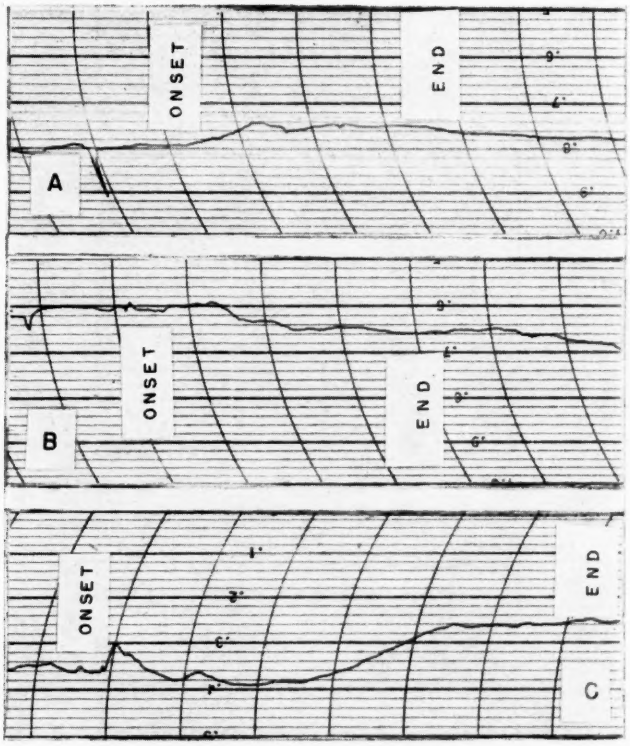

Fig. 5.—Tracings obtained by the direct current amplifier while the patients were made completely oblivious of pain during the uterine contractions by caudal anesthesia.

A. This tracing was made upon a patient in moderate early labor, and cervical dilatation was slow.

B. This patient was having firm contractions and the cervix was dilating rapidly.

C. This tracing was taken at the end of the first stage of a patient in a severe driving labor in which there was mild cephalopelvic disproportion.

Tracing *A* shows the drift of the instrument under laboratory conditions, with no electrodes on an individual but merely connected across a 10,000 ohm resistor. The 1½ millivolt standard was used to produce the standard deflection.

Tracing *B* (Fig. 6) shows two consecutive contractions and the interval on a patient without sedation.

Tracing *C* (Fig. 6) shows the same type of labor in a patient with caudal anesthesia.

Group Four.—Obtained by direct current amplifier at cesarean section with electrodes on the uterus.

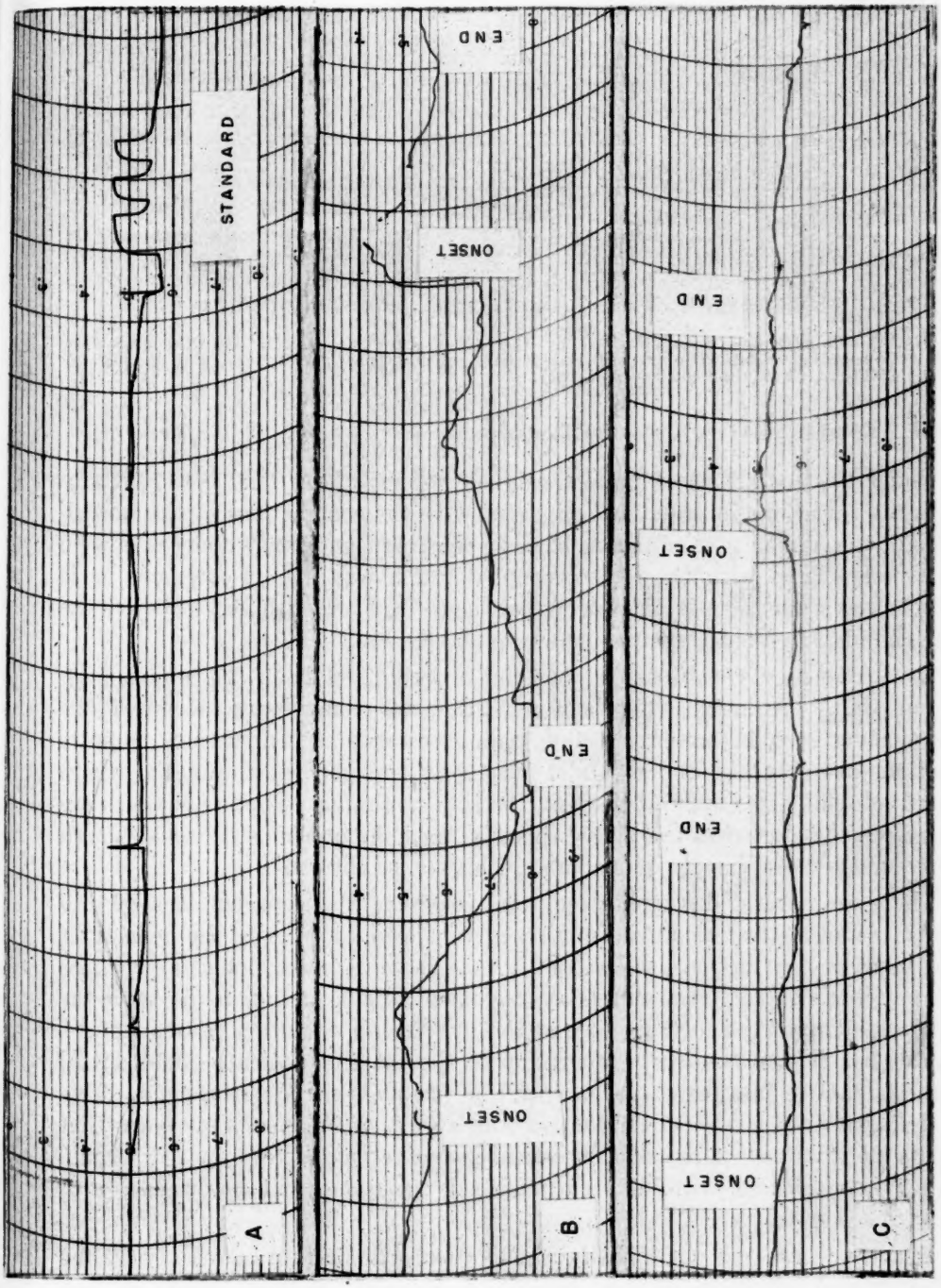

Fig. 6.—Tracings taken with the direct current amplifier.

A. The leads were attached across 10,000 ohms resistance to provide a control for calculation of "drift" inherent in the equipment. The area marked "standard" represents the deflection produced by the application of one and one-half millivolts across the input terminals.

B. This tracing represents successive contractions of the uterus in active labor. This patient had no sedation. The over-all picture is presented and the action of the recorder between contractions is evident.

C. This tracing is taken from a patient having the same type of labor but experiencing no pain because of the caudal anesthesia. Note the huge difference in the over-all pattern.

This curve (*A*) is an electrical deflection produced by a pituitrin-induced contraction. The patient was under light ethylene anesthesia and was given 3 minims of pituitrin intramuscularly.

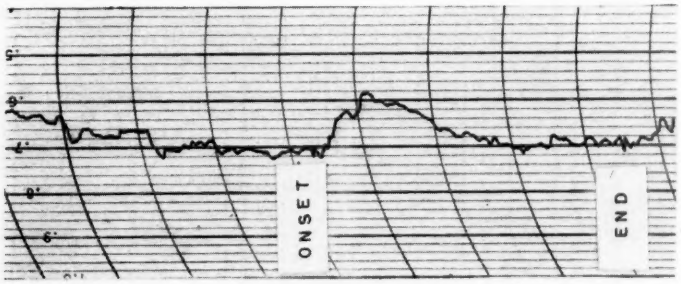

Fig. 7.—This tracing was obtained by the direct current amplifier directly from the uterus at cesarean section. The patient was lightly anesthetized by ethylene and a pain induced by pituitrin (3 minims intramuscularly).

Discussion

Under the conditions of this experiment we have been unable to find any significant variations in potential associated with the contractions of the smooth muscle of the human uterus during labor in the frequency range above one cycle per second. Trial with the electroencephalograph was not as extensive as is desirable but with the portable electrocardiograph, even with the leads on the uterus, no high frequency components were noted.

Low frequency variations in potential are obtained from the anterior abdominal wall. Although voluntary muscle factors may cause many of the large changes seen in patients feeling pain from uterine contractions, definite deflections are obtained under caudal anesthesia and general anesthesia, where striated muscle effects must of necessity be at a minimum. Similar changes are noted when the electrodes are placed directly upon the uterine surface, although they are much more sharply defined and of higher amplitude.

There are several disturbing features, however: the apparent lack of uniformity of the method of spread of this current over the uterus, the deflections noted between contractions, which rarely may have as much potential as those accompanying contractions, and other technical details having to do with the lack of stability of the instrument and the interfering voluntary muscle effects. Malpas[16] has shown by direct observation of the uteri of patients under spinal anesthesia that in late pregnancy the uterine fundus contracts in a mass. This and the pattern of electrical conduction which we have observed may mean that there is no constant pacemaker or specific conduction pattern in this organ. Further investigation with different electrode positions will be necessary to clarify this point.

Exactly where this method of investigation will fit into the study of the physiology and pathology of labor remains to be seen. It does seem to be true that weak and inconsequential contractions produce less voltage than severe contractions. The pattern of the change in potential both during and between contractions is too confusing at this time even to allow speculation.

Summary

Contraction of the uterine muscle during labor in the human is accompanied by changes in potential of low frequency and voltage.

Voluntary muscular activity, the apparent lack of identical or even similar conduction patterns, and the technical inherent difficulties of the amplification of direct current all make a great deal of investigation necessary before the procedure can be properly evaluated in respect to its status in the labor problem.

The authors wish to thank Dr. G. J. Ellis, Dr. J. B. Sheffery, and Dr. Catherine Johnson of Providence Hospital, Washington, D. C., Dr. Thomas Leonard and Dr. William Lady of Gallinger Hospital, Washington, D. C., and Dr. J. W. Pearson of the United States Naval Dispensary, Bellevue, D. C., for help on this problem.

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THE FOURTH STAGE OF LABOR*

An Account of the Physiology and Clinical Aspects of the Postpartum Uterus During the First Postplacental Hour

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"There is no more startling or fearsome thing in the practice of obstetrics than an unexpected, serious, postpartum hemorrhage." (Titus[1])

THE sequence of intrauterine events which transpire during the postplacental hour comprises a distinct physiologic and clinical entity. Their collective recognition as the "fourth stage of labor" would help save the lives of those mothers who die of mishandled postplacental hemorrhage and spare the survivors the complications of sepsis and anemia that lie in its wake.

As the sulfonamides and antibiotics seal the doom of puerperal infection, puerperal hemorrhage will eventually take first place among the causes of maternal mortality. And as the attempts to combat puerperal hemorrhage gain in momentum, the critical first postplacental hour will necessarily have to be accepted as a normal part of every labor; for, as a series of individual but interrelated physiologic components, the fourth stage of labor will have to be recognized and treated with understanding, lest one of its components rebel under maltreatment, go berserk, and cause destruction.

Dieckmann,[2] in 1935, stated, ". . . obstetric hemorrhage is of great import, and despite our voluminous and occasional enthusiastic reports of the treatment of these various conditions, the mortality has not decreased in the past twenty years. What is the explanation for this appalling mortality?"

A five-year maternal mortality study for the years 1935 to 1940 in the city of Buffalo[3] showed hemorrhage to be still in the background; true, it caused the death of 64 mothers, which was 20 per cent of all maternal deaths; but it was second only to puerperal sepsis which, in the early days of sulfonamide therapy, was still able to be queen of the causes of maternal death. As in Buffalo, so throughout the world, sepsis served to distract obstetricians from the "broad stream of blood" that ran through the morbidity and mortality statistics of postpartum pathology ever since Man exchanged a rib for the uterovaginal tract.

In a later study, conducted in the Borough of Brooklyn of the City of New York, the trend from sepsis to hemorrhage is clearly seen. This seven-year report of the major causes of maternal mortality in that densely populated part of Greater New York, from 1937 to 1943, shows that hemorrhage superseded both infection and toxemia (Fig. 1); it was thus concluded by Gordon, that "hemorrhage is the outstanding controllable factor in maternal mortality."

On the basis of that study, Gordon[4] contended that "preventive measures for reduction of maternal mortality will produce greater results if emphasis is placed on hemorrhage rather than infection. At present, hemorrhage is the most important cause of maternal death, and probably the most common as well."

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*This paper is based on observations made by the author while he was Resident Physician in Obstetrics and in Obstetrics and Gynecology at the New York City Hospital, New York Beth Israel Hospital, and at the Buffalo General Hospital.

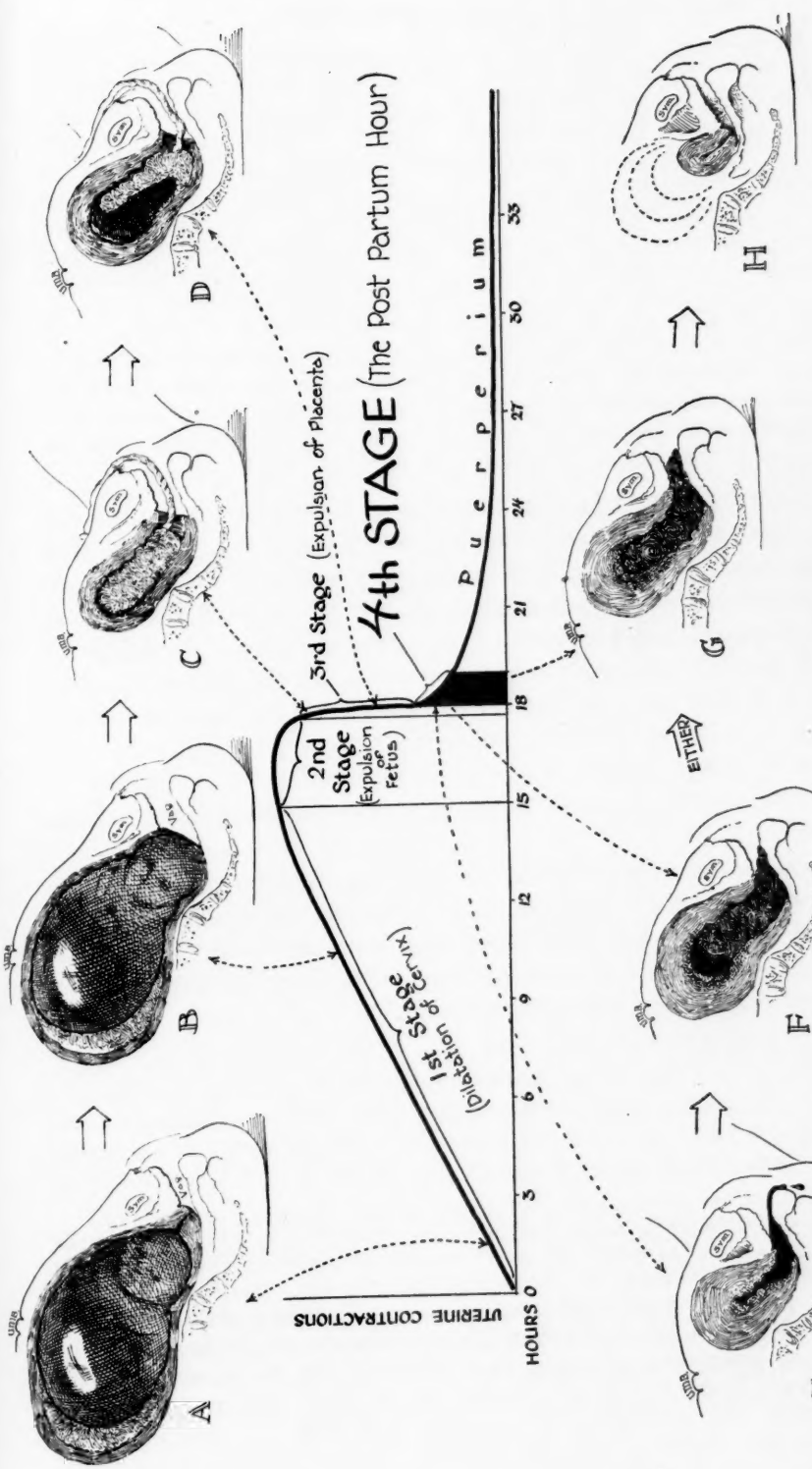

Fig. 1.—The stages of labor with special reference to the postpartum hour as the fourth stage of labor.

TABLE I. MAJOR CAUSES OF MATERNAL DEATH
BROOKLYN, 1937-1943

YEAR	INFECTION	TOXEMIA	HEMORRHAGE
1937	27	26	29
1938	27	18	27
1939	30	12	14
1940	18	10	28
1941	10	8	20
1942	25	22	30
1943	13	14	60
Total	150	110	208

A recent study of all maternal deaths in the viable period of pregnancy in the Borough of Manhattan of the City of New York, by a special Committee of Maternal Welfare, "reveals the startling fact that more than one-half of all maternal deaths during this period of pregnancy are due directly to hemorrhage or that hemorrhage is a factor leading to subsequent low vitality and eventual septic death . . . most of the deaths occurring post partum."[5]

Puerperal hemorrhage may be ante partum, post fetal, or post placental (post partum). The mechanism and management of hemorrhage in the first three stages have been adequately explained and classified. This paper, in presenting for consideration the "fourth stage of labor," necessarily deals with postplacental hemorrhage, and proposes to help combat it by recognizing the first postplacental hour as a separate and distinct phase of the process of labor. By so recognizing that hour as a physiologic entity having its own normal pattern and subject to its own peculiar aberrations, it is hoped that the postplacental hour can be more intelligently and uniformly handled, especially by those who too often assume that the labor is over with the delivery of the placenta.

Labor, as it is now universally understood, refers to the three classic stages: (1) stage of effacement and dilatation of the cervix; (2) stage of expulsion of the fetus, and (3) stage of placental separation and expulsion. As defined by Beck,[6] labor is that "process by which the mature products of conception are separated and expelled from the maternal organism."

DeLee,[7] however, defines labor more broadly, as "a function of the female organism by which the product of conception is expelled from the uterus through the vagina to the outside world *and the regressive metamorphosis of the genitalia started.** The latter part of DeLee's definition is not incompatible with, and is, in fact, a step toward the recognition of a fourth stage in the epic process of parturition.

Williams[8] almost conceded the presence of a fourth stage of labor, when he stated that "from a practical point of view, the hour following the delivery of the placenta is just as important as the actual third stage. Indeed, these *two periods** may be said to be more dangerous to the mother than *the other stages of labor,** as is reflected in the immediate danger due to hemorrhage and the more remote risk of puerperal infection, as a result of the management of the patient at this time. These complications may prove fatal, or necessitate prolonged convalescence, but fortunately are often preventable."

In a review of the literature, the first mention of the "fourth stage" that could be found was made by Leff,[9] who suggested that the interval between the

*Italics mine.

delivery of the placenta and the time the mother is put to bed in her room be known as the "fourth stage of labor." However, the interval between the delivery of the placenta and the time the mother is put to bed in her room is too variable to be used as a time ordinate against which to plot vital physiologic events. Furthermore a "norm" for the average fourth stage will have to be arrived at after a study of thousands of cases, just as "norms" have been ascertained for the average first, second, and third stages of labor in primiparas and multiparas. I propose that the first hour following the delivery of the placenta be considered as the normal duration of the fourth stage of labor, until further exhaustive studies will either add or detract a few minutes from the already rather arbitrarily accepted "postpartum hour."

With the average physician, in the average delivery room, the hour immediately following the delivery of the placenta has belonged neither to labor nor to the puerperium. It is the time when the patient, often in the throes of postanesthetic retching and vomiting, is stripped of the bloody drapes and transported to a stretcher amidst the nervous bustle of impatient nurses whose one thought is to get the patient off the table and into her room. Thus, an overconfident nurse who is ignorant of the physiology of the postplacental period and, therefore, its proper management, is a threat to the safety of the mother, especially when the postplacental hour is exclusively entrusted to her.

It is during this forgotten hour—this "no man's land" between labor and the puerperium—when most of the deaths caused by obstetric hemorrhage take place. These deaths occur because of the blind faith placed in a few quick clot-expelling jabs at the uterus, and in a cubic centimeter of ergot or pituitary preparations. They also occur because there are no adequate facilities for immediate blood transfusion, or because recognition of the necessity for blood transfusion comes too late.

This, of course, is not the procedure followed in our best clinics and hospitals, but it is, unfortunately, the procedure followed in the great majority of the delivery rooms and private dwellings in this country today. Beecham,[10] from a study of postpartum hemorrhage in Philadelphia for the years 1931 to 1936, concluded that "methods employed in the treatment of postpartum hemorrhage were often haphazard and lacking in uniformity."

By recognizing the hectic postplacental hour for its physiologic singularity and clinical importance, and by including it as an important fourth entity alongside its three predecessors in the labor records, the obstetric attendant would be impressed with the fact that the delivery is not yet over with the expulsion of the placenta. The early postplacental danger period would thereby be converted from a haphazardly handled to a scientifically handled and dignified hour. Such recognition of the first postplacental hour as the "fourth stage of labor," with its incorporation as such into the clinical labor records, would protect the mother, render an obstetric lesson to medical students and nurses, and serve as a guide and a check on the obstetrician, who would have to record his observations during the fourth stage, just as he has had to record his observations on the previous three. "The fourth stage" would lend needed dignity to the treacherous first postplacental hour, and instil more respect for its chief complication, postplacental hemorrhage, which is so dreaded and mishandled in inexperienced hands.

Physiology of the Fourth Stage of Labor*

The fourth stage represents the tapering off of the actual process of labor. (See Fig. 1.) It is the natural decrudescence of the process whose acme is attained with the expulsion of the products of conception, and whose increment is built up by many hours of contractions, which steadily mount in frequency and intensity. If the course of labor were graphically charted and compared with a graphic representation of the labor pain itself, it would be seen that the whole process of labor resembles each of its individual components, in sharing with them the characteristics of a gradual increment, a sustained acme, and a rapid decrudescence.

The normal fourth stage of labor consists of two main parts: (1) the contractile phase, and (2) the hemorrhagic phase. Both phases are, of course, interrelated and inseparable, but for purposes of lucidity will be described separately.

Contractile Phase

A. Stage of *uterine myotamponade* (immediate uterine contraction).

B. Stage of *uterine thrombotamponade* (secondary relaxation with formation of placental site sinuosoidal and intrauterine hematomas).

C. Stage of *myouterine indifference.*

D. Stage of *fixed myouterine contraction.*

A. *Myotamponade.*—Immediately after the fetus is expelled, the uterus contracts and decreases in size; as the placenta separates, the uterus rises slightly and becomes more globular (Calkins),[11] only to further decrease in size after the delivery of the placenta; the uterus then usually contracts down to a point halfway between the pubis and umbilicus. Sometimes it descends to an even lower level, especially in a primipara under the influence of oxytocics. However, in multiparas, or even in primiparas under deep anesthesia, the immediate contraction stage may be very transitory, and the uterus (which is now usually slightly dextroverted) may rise to the umbilicus, or even above, shortly after placental delivery.

In the stage of immediate uterine contraction, tamponade is achieved by the compression, kinking, and twisting of the uterine vessels which are enmeshed in the multiplaned divagations of the myometrial whorls. *This is the first line of defense against postpartum hemorrhage.*

B. *Thrombotamponade.*—Thrombotamponade of the postpartum uterus depends upon (1) the thrombi in the large uteroplacental blood vessels, and (2) the intrauterine hematoma or hematomas with which the placental-site vessels may or may not be continuous. In the words of Teacher,[12] "the interior of the uterus in the first place is occupied by a thick mass of blood clot. This is easily stripped from the decidua vera but is more adherent at the placental site, as the clots are continuous with the thrombi in the torn ends of the large uteroplacental blood vessels."

The clot that begins to form in the cavum of the uterus after the placenta is expelled partially or completely fills the uterus as it gradually relaxes and rises again. After a gradual rise at the end of one hour, the uterus is at, or slightly above or below, the level of the umbilicus. The tamponading hematoma of the postplacental period, which is as important a mass to the fourth stage of labor as the placenta is to the third, is the *second line of defense against hemorrhage* in the early postplacental period when the sinuses of the placental

*The functional processes of the postplacental hour, as are here postulated, represent the natural series of postpartum uterine events unmodified by oxytocics or other drugs, unless otherwise specified.

site are but freshly thrombosed, and the stage of fixed contraction has not yet been reached. The myometrial contractibility on the one hand, and the stimulation by the pressure of the clot on the other, finally attain a state of equilibrium, which may be called, "myothrombal equilibrium."

It is of the utmost importance to recognize the function of the single intrauterine hematoma or the continuous multiple hematomas as nature's tampon which, together with the contraction, retraction, and kinking of the uterine muscle fibers, cut off uterine hemorrhage by a simple pressure mechanism. In cases of strong and prolonged muscle contraction, there may be little or no caval clot. But in cases of mild contraction due to atony, the caval clot is of great importance, and its integrity must not be insulted by uterine squeezing which results in its partial or complete expression.

An excessively large placental site or the presence of the placental site in the passive lower uterine segment may be factors in inefficient uterine autothrombotamponade and myotamponade. In placenta previa, the fourth stage is therefore rife with greater risk, owing to the failure of adequate placental site contraction. In some hospitals, therefore, it is a rule to pack the uterus routinely after a placenta previa or marginalis delivery, as a prophylactic against hemorrhage.

C. *Myouterine Indifference.*—After expulsion of the placenta and subsequent autotamponade of the uterus, it would be a safe attitude to consider the uterus to be indifferent or apathetic from the contractile standpoint, for at least one hour; that is, it will remain in a state of isotonicity, hypotonicity, or hypertonicity, and may indeed transiently alternate between the three.

If there be frequent brisk massage with expression of clots and resulting temporary contraction (but often secondary relaxation), the stage of uterine indifference is prolonged; for the uterus will contract with each stimulation, and very often relax again when stimulation is ceased, to a point of isotonicity and then possibly hypotonicity, without the benefit of the myothrombal check because the clots have been expelled. For this reason, obstetricians who prefer to "squeeze the uterus dry," often order a tight binder over a suprafundal sandbag to control a fundus which was artificially overstimulated by hand and by injected oxytocic, and which was not permitted to achieve its own level. If, within certain limits, the uterus were permitted to rise and fill with clot, then heavy sandbags and tight binders would be unnecessary, and the unpredictable indifferent stage would be greatly shortened. Even when the uterus relaxes and rises, some degree of vascular compression still prevails, as the uterus rarely rises as high post partum as its height was before expulsion of the fetus.

The indifferent or apathetic uterus, even when undisturbed and permitted to fill with blood clot, may yet follow the alternating phases of contraction and relaxation with alternate expression of and refilling with clots; this is especially true when the patient coughs or vomits, or is jarred as in the movement from the delivery table to the stretcher cart, and from the cart to the bed. The obstetrician has no way of determining the final course which the typically vacillating postpartum uterus will take. Knowing the character of the fourth stage in the patient's previous labors might be of help. Guided by that information, if available, the obstetrician has but to gently palpate and stimulate the uterus with a force just below that which is required for the expression of clots, to watch, wait, and observe.

It would appear that it is unreasonable to expect a freshly emptied uterus to contract and remain contracted after hours of alternate contractions and relaxations. The alternating cycles of contractions and relaxations extending into the postplacental period and beyond, and often perceived by the patient as "afterpains," are the physiologic analogues of the labor pain itself, and are responses to the same unknown stimulus; they are a tapering off of the cyclically expulsive

process which we call labor, and which we have heretofore arbitrarily consigned to the period up to and including the delivery of the placenta, but not beyond.

The fourth stage of labor varies in character with the parity of the mother and with the length and quality of the previous three stages. The greater the parity, the greater the tendency to a weakly contracting, vacillating, or "indifferent" uterus. Thus, the administration of small amounts of posterior obstetric pituitary extract to a cephalopelvically proportioned multipara whose cervix is fully dilated and who is having weak pains five minutes or more apart, may serve to tone the uterus and prevent postplacental hemorrhage due to uterine "indifference." The more protracted the first three stages, the greater the tendency to uterine muscle exhaustion and resulting atony and hemorrhage. If, on the contrary, the labor has been of very brief duration, there is likewise an added danger of postplacental hemorrhage (the exact reason for this is unknown). Polyhydramnios, multiple pregnancy, and large fetus, by excessive distention of the uterus, also predispose to a bleeding fourth stage. Peckham and Kuder[13] have reported a higher incidence of postpartum hemorrhage in primiparas than in multiparas, but the same authors state that the incidence of postpartum hemorrhage is greater in operative than in spontaneous deliveries, and the higher incidence of operative deliveries in primiparas may account for the higher rate of primiparous postpartum hemorrhage in their series.

A weakly contracting and "indifferent" uterus may perhaps be compared with a heart decompensating because of myocardial weakness. Thus, a uterus which is deficient in elastic tissue[14] (such as a multiparous uterus might be prone to manifest as part of the aging process), and perhaps stretched, thinned, hyalinized, and fibrosed by previous labors and arteriosclerosis, and its powers of contractility thereby weakened, may be considered the analogue of a dilated heart. When a dilated heart has reached the limits of its contractility, the blood dams back, as it is not adequately propelled forward; when a "dilated" uterus has reached the limits of its contractility, the uterine contents (fetus and placenta) remain a longer time (uterine atony), and, once expelled, the second mass of uterine contents (caval hematoma) is allowed to expand and grow by bleeding within the confines of its own yielding walls. The uterus may then contract and expel blood clots, either under the influence of injected oxytocic, spontaneously by its own strength, or by manual expression; only, however, to frequently relax again, and to again distend with blood. If this vacillating process repeats itself often enough, the patient may exsanguinate herself. This exsanguinating process is aided by intermittent well-intentioned but overzealous, deep, manual abdominouterine massage.

It is perhaps as unphysiologic to express blood clots from the uterus as it is to blow one's nose during a nosebleed. The clot that forms in the nose of the street urchin is sometimes treated with greater respect than the caval hematoma in the uterus of the postpartum mother.

D. *Fixed Myouterine Contraction.*—The safe attitude is to assume that the uterus has never quite reached a state of fixed contraction for ten days, for cases of delayed postpartum hemorrhage have been reported up to ten days or more. However, the late hemorrhages are usually due to retained secundines, or to the bleeding sites of partial or focal placenta accreta.[15] Many cases of so-called "delayed postpartum hemorrhage" within a few hours post partum, are not delayed hemorrhages at all, but hemorrhages whose recognition is delayed.

In a normal fourth stage, the uterus should be firmly and irreversibly contracted by the end of the first postplacental hour. Many uteri will achieve fixed contraction in less time, especially the primiparous and secundiparous ones; some will require a little more time and yet be within the range of normalcy. The upper limit, as Williams suggested, might perhaps be an hour and a half.

Should the uterus continue to alternately contract and relax, or should the uterus undergo acute passive dilatation, then the fourth stage should be considered delayed and abnormal, and even more carefully followed. Failure to achieve the state of fixed contraction results in hemorrhage, or the immediate possibility of hemorrhage. The hemorrhage may be overt or concealed. When concealed, the hemorrhage is in the form of a caval hematoma which is tamponading; and, though it may gradually grow in size, it would be exsanguinating only if repeatedly expressed through the vagina, or lacking that outlet, if it escapes through the rent of a previously ruptured uterus.

Hemorrhagic Phase

The normal hemorrhagic phase of the fourth stage of labor concerns itself with two main types of physiologic hemorrhage, traumatic and atonic:

A. *Traumatic Hemorrhage*

1. Uterovaginal tract laceration bleeding (Component One)

B. *Atonic Hemorrhage*

1. The clotting hemorrhagic component (Component Two)
2. The nonclotting hemorrhagic component[16] (Component Three)

The Components of Normal Postpartum Hemorrhage.—Component One: Traumatic hemorrhage of the mild variety is physiologic. If a test tube be inserted into the vagina (above the episiotomy, if there be any) immediately after fetal but before placental delivery, a few cubic centimeters of clotting blood can almost always be collected; this is due to uterocervical-vaginal trauma.

Component Two: The next collectable blood sample is that hemorrhage associated with placental separation, and which continues following the atonic rise of the uterus after placental delivery, but before the uteroplacental sinuses have begun to thrombose. This blood sample clots very quickly, either because of some factor it contains which promotes clotting, or because it has already begun to clot while a part of the retroplacental hematoma, or while it made its way in its meandering trickle down the pathway of the uterovaginal tract.

Component Three: (The nonclotting component.)[16]

Shortly after the delivery of the placenta is completed, the uterus, even after it is contracted by oxytocics and external stimulation, will continue to ooze a nonclotting blood, either spontaneously or upon manual transabdominal uterine compression. This "nonclotting component of normal postpartum blood" is collectable up to twenty-four or more hours post partum. The blood, when collected in a test tube, does not clot even if kept for days; when the test tube containing the cellular sediment is agitated, the cells are easily resuspended homogeneously. (In any of these samples, especially the early ones, there may be present a small contaminatory clot from one of the antecedent clotting components of postpartum blood.)

The *"nonclotting component"* probably comes from the bleeding myometrium recently denuded of its decidua. The clotting component, which is associated with placental separation, is normally shut off with the twisting, kinking, compression, and thrombosis of the placental site vessels during the stages of myotamponade and thrombotamponade.

This normal *"nonclotting component"* of postpartum blood may be analogous with the nonclotting component of menstrual blood which this author believes also consists of two components, a clotting and a nonclotting. The same uterine enzyme which may be responsible for the failure of one of the postpartum blood components to clot may be responsible for the failure of one of the menstrual components to clot.

The normal postpartum hemorrhage of the "nonclotting component" may, in some respects, therefore, he considered as a kind of first, acute, menorrhagic menstrual period.

Comment

This presentation of the physiology of the fourth stage of labor is not offered in the fixed definitive sense; it is offered rather as a basis for further physiologic and pathologic research which will undoubtedly result in modifications of the present concept of the fourth stage of labor, especially in the present incomplete understanding of its polyhormonal control, and in its hematologic, histologic, and chemical ramifications.

Further physiologic investigation will probably show that two factors are in constant interplay in the contractile phase of labor, and that these two factors are as important in the fourth stage as in the initiation of the process of labor itself. These two factors are the contractogenic transmitters, which are probably hormones, of which the pituitary factor may be but one; and the contractile receptors, which are the muscle fibers, or special groups or bundles of muscle fibers arranged, perhaps, in a heretofore unrecognized myoneural conduction pattern as in the Pacemaker and Purkinje System of the heart. Pathology of either transmitter or receptor, or of a distant chemihormonal, local histopathologic, or intrinsic chemical block between the two would, in such a system, result in a failure to achieve normal, efficient, uterine contraction.

The anticlotting enzyme[17] of the uterus (which, if it exists, I propose it be called "hysterin") or the lack of or the neutralization of a certain clotting component, may explain the failure of a component of postpartum blood to clot. This nonclotting component may be the explanation for a nonclotting type of postpartum hemorrhage,[18] whose true basis may have erroneously been relegated to the category of "shock bleeding." The possibility of the existence of the latter mechanism in certain cases of postpartum hemorrhage, either alone or superimposed, is not denied, however.

Postpartum hemorrhage, when not due to uterovaginal tract trauma, may consist of a hemorrhage of (a) one of the clotting components, (b) the nonclotting component, or (c) a combination of any two, or all three.

Summary

1. A tapering-off of the process of parturition occurs during the postplacental hour; this decrudescence should be recognized as the "fourth stage of labor."

2. The fourth stage of labor is a physiologic and clinical entity.

3. The physiology of the fourth stage of labor is postulated, the two main physiologic phases being:

I. *The Contractile Phase*
   A. Stage of *"Uterine myotamponade"*
      (immediate uterine contraction).
   B. Stage of *"uterine thrombotamponade"*
      (secondary relaxation with formation of placental site sinusoidal and intrauterine hematomas).
   C. Stage of *"Myouterine indifference."*
   D. Stage of *"Fixed myouterine contraction."*

II. *The Hemorrhagic Phase*

A. *Traumatic hemorrhage*

1. Uterovaginal tract laceration bleeding. (Component One.)

B. *Atonic Hemorrhage*

1. The clotting hemorrhagic component associated with placental separation. (Component Two.)
2. The nonclotting hemorrhagic component probably arising from denuded myometrium.[16] (Component Three.)

4. Both the contractile and hemorrhagic phases are simultaneous and interrelated.

5. The official recognition and physiologic appreciation of the fourth stage of labor would result in a reduction of mortality from postpartum hemorrhage, which is assuming first place among the causes of maternal mortality.

6. A questionnaire concerning the fourth stage of labor should be part of every labor record.

7. The normal *"nonclotting component"*[16] of postpartum blood may be analogous with the nonclotting component of menstrual blood which this author believes also consists of two components, a clotting and a nonclotting. The same uterine enzyme[17] which may be responsible for the failure of one of the postpartum blood components to clot may be responsible for the failure of one of the menstrual components to clot.

8. Postpartum hemorrhage, when not due to uterovaginal tract trauma, may consist of a hemorrhage of (a) one of the clotting components, (b) the nonclotting component, or (c) a combination of any two, or all three. "Shock bleeding"[18] may be a superimposed late complication.

The author wishes to thank Mr. Melford Diedrick of the Buffalo General Hospital for the illustration.

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PATHOLOGIC FINDINGS IN GENITAL BLEEDING TWO OR MORE YEARS AFTER SPONTANEOUS CESSATION OF MENSTRUATION

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IN 1930, 157 cases of genital bleeding occurring on the Gynecological Service of the Johns Hopkins Hospital were studied from a clinico-pathologic viewpoint and reported by TeLinde.[1] He found malignancy to be the cause of the bleeding in 55.9 per cent. In 1937, he[2] augmented the series and reported on 349 cases, occurring on the service between Jan. 1, 1919, and Jan. 1, 1935. In the larger series he found the incidence of malignancy to be 53 per cent. The literature up to 1941 reveals an alarmingly high proportion of malignant to benign causes of the bleedings.

TABLE I

YEAR	AUTHOR	LOCALITY	NO. OF CASES	PER CENT MALIGNANCY
1930	TeLinde[1]	Johns Hopkins Hospital, Baltimore	157	55.9
1931	Ducuing[3]	Toulouse Cancer Clinic, France	326	90.0
1932	Kanter and Klawans[4]	Presbyterian and Cook County Hospital, Chicago	98	68.4
1933	Schultze[5]	University of California Hospital, San Francisco	315	68.0
1933	Geist and Matus[6]	Mt. Sinai Hospital, New York City	182	57.5
1935	Norris[7]	University of Pennsylvania, Philadelphia	189	53.0
1937	TeLinde[2]	Johns Hopkins Hospital, Baltimore	349	53.0
1938	Keene and Dunne[8]	University Hospital, Philadelphia	782	60.0
1938	Taylor and Millen[9]	Roosevelt Hospital, New York City	406	63.0
1941	Geiger[10]	Loyola and Cook County Hospital, Chicago	395	81.0

Within the past several years estrogens have been used and misused on a tremendous scale. Attention has been called to the misuse by Scheffey[11] and others. As a result, serious organic genital lesions are often prevented from being properly evaluated. In addition, much genital bleeding is artificially induced by the use of estrogens, particularly stilbestrol. Offsetting the effect of this enthusiasm for hormones, the medical journals have published many articles, warning the profession of the sinister significance of postmenopausal bleeding. In view of these cross currents of therapeutic hyperenthusiasm and public enlightenment, it seemed appropriate to restudy the cases of postmenopausal bleeding in our clinic.

This study was undertaken on 514 cases occurring on the private and public ward services and in the dispensary of the Johns Hopkins Hospital. In order

to obtain as nearly as possible a real cross-section impression of postmenopausal bleeding occurring in the Clinic, women referred for treatment for previously proved carcinomas were excluded from this study. The distortion in incidence which would arise from including such cases is illustrated by the report in Table I from the Toulouse Cancer Clinic, where 90 per cent of the cases of postmenopausal bleeding were found due to cancer. A comparison of this figure, with the statistics from other clinics, clearly indicates that it does not represent the incidence of malignancy on a general gynecologic service.

In surveying the literature, it is apparent that there is much difference of opinion as to just what constitutes the postmenopausal period. TeLinde limited his cases to those in which there was a reappearance of bleeding after a year of amenorrhea. Most authors fail to mention their time limit. In this study we have made an arbitrary limit of two years' amenorrhea. Since this limit would rule out many cases of benign bleeding shortly after the cessation of the normal menses, it should increase the incidence of malignancy.

Material

There were 514 cases, occurring over a period of seven and one-half years, which have met the two requirements:

1. Initial pathologic diagnosis must have been made in the Department of Gynecological Pathology.

2. At least two years must have elapsed before genital bleeding recommenced.

These cases were collected in the following manner:

1. The operation files were scanned for patients whose tentative operative diagnosis was "postmenopausal bleeding." The names of all women 45 years old or over were noted and the hospital or office records studied for menstrual data. Among 13,959 operations, 402 were performed on women who had postmenopausal bleeding, representing 3.3 per cent.

2. The records of the Department of Gynecological Pathology were examined for menstrual data. The remaining 52 cases of this series were obtained from this source and represent cases which were either too far advanced to have reached the operating room for application of radium, or were referred elsewhere for treatment. In the seven-and-a-half year period covered by study, a total of 16,742 pathologic case reports were reviewed.

3. A single cause for the bleeding was determined in each case from a combined study of the history, and clinical and pathologic reports. Multiple causes were avoided, and in borderline cases the history and material were reviewed again for final decision.

4. With few exceptions the patients received a complete diagnostic study which included the following: (a) general physical examination. (b) gynecologic examination with visualization of the cervix and vagina, and pelvic bimanual palpation. (c) digital examination of the anus and rectum; proctoscopy, if indicated. (d) Examination of catheterized urine. If there were urinary symptoms and persistent abnormal microscopic findings, cystoscopy, catheterization of the ureters, differential phthalein, and retrograde pyelography were carried out. (e) Routine hemoglobin and white blood cell count. Complete blood study was done if there was an unexplained anemia. (f) Biopsy of the cervix regardless of its appearance. (g) Curettage of the cervical canal and uterine cavity.

Exceptions to the above were made as follows: (a) In cases of pyometra when curettage and biopsy were postponed until the pyometra had been drained by dilatation of the cervical canal. Two cases of pyometra subsequently found to have endometrial carcinoma received radical surgery without preliminary curettage. (b) In one case of suspected carcinoma of the endometrium panhysterectomy and removal of adnexa were performed without preliminary curettage. (c) Occasionally biopsy of the cervix was omitted in the private practice of visiting gynecologists if the cervix appeared normal. (d) Curettage of the uterine cavity was omitted in cases of definite epidermoid carcinoma of the cervix with necrosis and infection.

TABLE II. PATHOLOGIC FINDINGS ACCORDING TO LOCATION

Vulva:	Carcinoma		2
	Melanosarcoma clitoris		1
	Ulcer, nonspecific (not granuloma)		2
Urethra:	Carcinoma		5
	Caruncle		10
	Prolapse		2
	Urethritis		1
Vagina:	Carcinoma		1
	Vaginitis, senile		60
	Granuloma inguinale		1
	Trauma		5
	Pessary		5
Cervix:	Carcinoma		104
	Polyp		37
	Prolapse		35
	Cervicitis marked		36
Uterus Corpus:	Carcinoma		58
	Sarcoma of endometrium		2
	Sarcoma in myoma		2
	Myoma, submucous		18
	Polyp, endometrial		18
	Hyperplasia of endometrium		20
	Endometritis, pyometra		6
Tube:	Carcinoma		1
	Tuberculosis		1
Ovary:	Malignancy		
	Papillary cystadenocarcinoma	3	
	Medullary carcinoma	1	9
	Krukenberg tumor	2	
	Granulosa-cell tumor	3	
	Benign		
	Papillary serous cystadenoma	1	
	Serous cystadenoma	1	4
	Pseudomucinous cystadenoma	2	
Bleeding probably from estrogen therapy:			12
Unknown cause, including seven with probable recrudescence of ovarian function:			56
			514

Since any bleeding from the female genitals was included in this study, lesions of the vulva and urethra are found in the tabulations. There were a number of cases in which the bleeding on initial physical examination was thought to come from atrophic vaginitis, a caruncle, or cervical erosion, but on complete study was found to issue from carcinoma of the cervix or a lesion higher in the tract. The point cannot be too strongly emphasized that costly mistakes will occur if one jumps to the conclusion that easily detected superficial lesions are responsible for the bleeding.

In Table II certain points are worthy of more detailed comment.

Vulva.—The bleeding from a nonspecific ulcer occurred in a white woman who was suffering from pruritis. The blood Wassermann was negative and a curettage revealed no other cause for bleeding. The remaining cases need no comment.

Urethra.—The case with urethritis had definite bleeding from a urethra which seemed not to be prolapsed and did not have a caruncle. Biopsy of the granular mucosa confirmed the clinical impression.

Vagina.—Atrophic vaginitis is indicated as a cause of bleeding when there was obvious bleeding from a thin, smooth vaginal mucous membrane, and when curettage of the cervical canal and uterine cavity revealed no other possible source of the bleeding. The presence of bleeding from an atrophic vaginal mucous membrane is not considered a license for omission of curettage and biopsy of the cervix. The woman with granuloma inguinale was bleeding profusely from a vaginal extension of the process. There are only five cases in this series where the bleeding was attributable to vaginal irritation from a pessary. There were three women who bled as a result of hot douches, and one who said she had "fallen off a hayrick." All of these had atrophic vaginitis which had caused no trouble until traumatized. The woman with the retained suture had had a vaginal plastic operation elsewhere one year previously. Bleeding stopped after the black silk suture was removed.

Cervix Uteri.—Prolapse of the cervix is listed as a cause when there was an ectropion of the endocervical mucosa or a decubitus ulcer bleeding on examination. These lesions should always be biopsied, for there were three cases in which cervical carcinoma occurred in a prolapsed cervix. Chronic cervicitis is not commonly recognized as a cause for bleeding. In this series, however, 36 cases were encountered in which blood was seen coming from the cervical portio, and no other source could be found on complete examination.

Corpus Uteri.—Hyperplasia of the endometrium is listed here among causes of postmenopausal bleeding and there were 20 such cases. Bleeding for the most part had been scanty and intermittent. The actual source of the bleeding is not easily evaluated, although four of the 20 had definite small endometrial polyps, and ulceration of the surface epithelium may have been a factor. The immediate cause of bleeding is not established in the other cases. In 13 of the 20 cases there had been more than four years of amenorrhea before hemorrhage recommenced. The average age at the time of bleeding was 54 years. The oldest was 67, the youngest 42 years. There are six who were over 60 years of age.

In 18 cases bleeding is ascribed to endometrial polyps. Two of these were associated with benign hyperplasia but were not included in that group because the polyps were large and grossly showed bleeding ulcerated surfaces.

Marked chronic or subacute endometritis was found in the curettings from six women who had no other source of bleeding. Of these there were four who had gross pyometra, and hence only an initial dilatation of the cervix was done, followed later by curettage when the discharge had subsided. There are five cases of endometrial carcinoma associated with pyometra which are not included here because of the more significant causal lesion.

Submucous myoma's caused postmenopausal bleeding in 18 cases. In two of these there was extrusion of the myoma through the cervix, and one of these had had a similar submucous myoma removed vaginally four years earlier, two years before her menopause. In this group of 18 cases only one of the women had had menorrhagia or metrorrhagia toward the close of her menstrual life. This finding is in accordance with the point brought out in 1940 by TeLinde[12] that some myomas may become submucous during involution of the uterus after the menopause. In some of our cases this apparently occurred after the age of 60 years.

Tube.—Primary carcinoma of the tube, a rare disease, occurs once in this series. A 58-year-old woman began vaginal bleeding eleven years after the menopause. The bimanual examination was thought to reveal nothing in the adnexal regions. On curettage, atrophic endometrium was obtained. Bleeding continued for six weeks. Another curettage was done. At the time of this operation a mass was felt in the left adnexal region. Because of the patient's age, the continued bleeding and the presence of an adnexal mass not previously observed; the operator, thinking that there was an ovarian tumor, performed a laparotomy, removing the entire uterus and adnexa. The left tube was swollen and, on microscopic study, was found to contain adenocarcinoma. Bleeding in this case must have come from the tube. Careful re-examination of the curettings revealed no suspicious cells.

In the single case of tuberculous salpingitis, a colored woman 59 years of age began having leucorrhea and slight vaginal bleeding after fifteen years of amenorrhea. A curettage after two years of spotting yielded insufficient endometrium for diagnosis and the cervix was atrophic. She died several months later, and at autopsy was found to have tuberculosis of the right Fallopian tube. This was the only apparent cause of the bleeding.

Ovary.—Tumors of the ovary, malignant and benign, were associated with genital bleeding in 13 cases. In the nine patients who had malignant tumors there were six who had extension of the carcinoma to the tube or uterus, probably accounting for the hemorrhage. An endocrine cause of bleeding may be postulated in the three granulosa-cell tumors. Of the four benign tumors, the cause is obscure, although one had an endometrial polyp which may have caused the bleeding.

Estrogen Therapy.—There are twelve women in the series who had received some form of estrogen which is considered a probable factor in the postmenopausal bleeding. Stilbestrol had been given to seven, amniotin, estrone or theelin to four, and in one case the medication is not stated. Curettings in two of the stilbestrol group showed the histologic picture of benign hyperplasia. One woman who was given an implantation of 50 mg. of estrone subcutaneously four years after her last period, bled one month later. Curettings showed secretory glands, and the tissue had the appearance of menstruating endometrium. It cannot be proved or disproved whether the estrone was a factor in the bleeding, but the secretory endometrium must signify some corpus luteum activity in her ovary. For the most part, in these hormonal therapy cases there was relatively little endometrium obtained.

It is our practice to carry out curettage in every case of abnormal bleeding following estrogen therapy. None of the 12 cases of this group was found to have carcinoma of the cervix or endometrium. This, however, is a small group, since relatively few women receive estrogen two or more years past the cessation of menstruation. During this survey, however, we noted several instances of carcinoma in estrogen-treated women whose period of amenorrhea was less than two years. We do not conclude from this that estrogen possesses carcinogenic powers, but rather that this was due to the ill-advised use of estrogen as a substitute for diagnostic curettage in abnormal bleeding before the patients reached the hospital.

Bleeding of Unknown Etiology.—In 56 cases (10.9 per cent) no satisfactory pathologic explanation of the bleeding was found. In six cases it is believed that a recrudescence of ovarian function may have been a factor. Except for one of these, whose endometrium showed secretory activity, this impression is based solely on the history of recurrent bleeding. The endometrium of the others was scanty in amount. In trying to establish the source of bleeding, it must be remembered that pedunculated submucous myomas and polyps of the endometrium may be missed on curettage. It is quite possible that some of

the 56 cases where bleeding was unexplained might have had small submucous myomas or polyps, since only one of the group had a hysterectomy.

Since hypertension is occasionally mentioned in discussion of abnormal bleeding, the blood pressures of individuals whose bleeding is unexplained were compared with those of groups with submucous myomas, polyps, and endometrial hyperplasia. No appreciable difference could be found. The average pressure was 151/85. In the laboratory, during its fifty-two years of existence, we have not observed a single case of "uterine apoplexy" in a nonpregnant uterus. Any less obvious manifestation of hypertensive uterine bleeding would test a pathologist's credulity.

TABLE III. PROPORTION OF MALIGNANT TO BENIGN LESIONS BY ORGANS

	TOTAL NUMBER	MALIGNANT	BENIGN
Vulva	5	3 (60%)	2 (40%)
Urethra	18	5 (27.8%)	13 (72.2%)
Vagina	72	1 (1.4%)	71 (98.6%)
Cervix	212	104 (49.1%)	108 (50.9%)
Corpus	124	62 (50%)	62 (50%)
Tube	2	1 (50%)	1 (50%)
Ovary	13	9 (69.2%)	4 (30.8%)
Estrogen therapy	12	0 (0%)	12 (100%)
Unknown	56	0 (0%)	56 (100%)
Total	514	185 (36.1%)	329 (63.9%)

Discussion

Race.—In the group there were 154 (30 per cent) Negro and 360 (70 per cent) white patients. Bleeding from prolapse of the cervix occurred only three times in the Negro patients, as compared with the 32 white patients. This is commensurate with our experience that prolapse in Negro women is rare.

Age at Menopause.—The average age at the time of cessation of menstruation, used synonymously with "menopause" in this paper, was 47.8 years. Norris found 47.5 years the average age in 200 cases. There were 26 women, 5 per cent, whose periods stopped before the age of 40 years. Of these, 18 were white and eight were Negro. This is in proportion to the total number of white to Negro patients in the series. The earliest menopause occurred spontaneously at the age of 25 years in a white woman who began irregular bleeding at 44 years and was found to have adenocarcinoma of the corpus at 50 years of age.

Of the 25 patients with menopause before the age of 40 years, there were four who had undergone surgery previously. One had stopped menstruation after a simple cesarean section when she was 36 years of age. She bled from a submucous myoma nine years later. The other three had stopped two, nine, and seventeen years after partial or complete removal of an ovary.

There were 215 women, 42 per cent, who stopped menstruating after the age of 50 years. There were 37 (7 per cent) who were 55 years of age or older. The oldest patient at the menopause was a white woman 59 years of age.

Relation of Age at Menopause to Cause of Postmenopausal Bleeding.—Although the number of cases in each group is too small to justify a statistical conclusion, the figures suggest a curve pattern that warrants further evaluation. The cases are divided into groups according to the age at the time menstruation ceased. The majority, 451 (86 per cent) fall between 40 and 55 years. Malignancy was responsible for bleeding in 33 per cent of these cases.

In sharp contrast to this middle group is the small group of women who stopped menstruating earlier than 40 or later than 55 years of age. There are only six who stopped before they were 35, but, of these, four (67 per cent) had malignancy. None had had an operation that might have brought on a premature menopause. Carcinoma of the endometrium occurred 12 times (60 per cent), compared to only eight benign causes. One of these had carcinoma of the urethra, another a granulosa-cell tumor of the ovary with liver metastases, six cervical carcinoma, two endometrial carcinoma, and one had sarcomatous degeneration of a myoma. Of 37 women who stopped menstruation after the age of 55 years, there are 18 (49 per cent) who had malignancy. These consist of one carcinoma of the endometrium, one sarcoma of unknown etiology in the pelvis, 12 cervical, and four endometrial carcinomas.

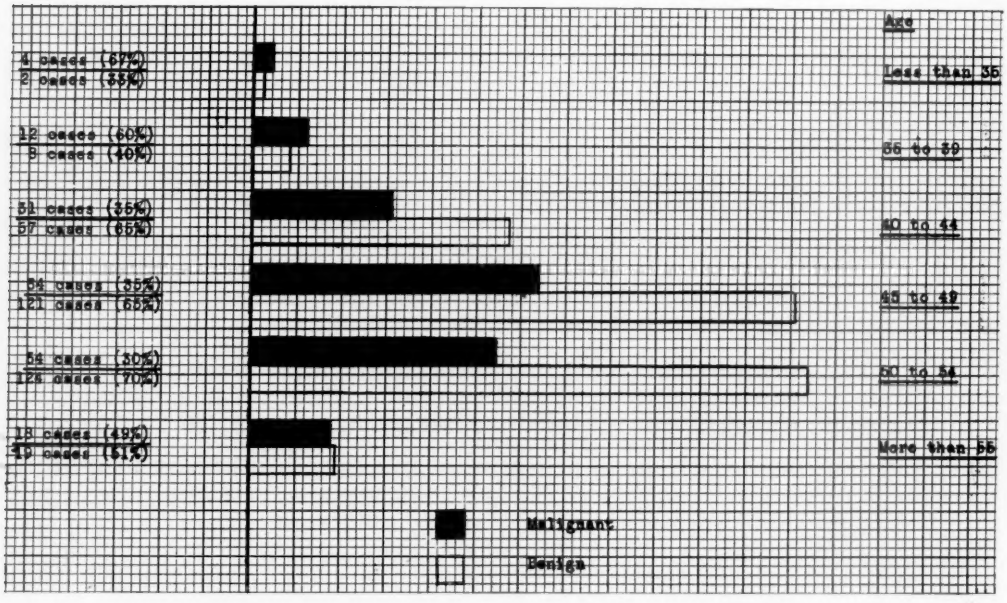

Fig. 1.—Proportion of malignancy according to age at the time the menopause occurred.

The question at once arises as to whether or not this varying proportion of malignancy to nonmalignancy according to age at the menopause is more apparent than real. It is to be expected that with increasing age there would be an increasing proportion of malignant to benign lesions, and this seems true when the ages at the time of diagnostic operation are tabulated in groups of five-year periods.

Duration of Amenorrhea Before Bleeding.—The length of time elapsing between menopause and onset of genital bleeding varies from two years, arbi-

TABLE IV. AGE AT CURETTAGE

	LESS THAN 50	50-55	55-60	60-65	65-70	MORE THAN 70
Malignant	13 (30%)	28 (26%)	48 (40%)	36 (40%)	33 (45%)	24 (53%)
Benign	30 (70%)	79 (64%)	71 (60%)	54 (60%)	40 (55%)	21 (47%)

trarily set as the definitive minimum, to thirty-five years. No correlation is found between the length of amenorrhea and the cause of postmenopausal bleeding. The average duration of amenorrhea for the entire group is 10.1 years.

Duration of Bleeding.—Duration of postmenopausal bleeding gives no indication of the responsible lesion. Approximately 5 per cent bled for a week or less before operation. Another 5 per cent bled for ten years or longer. The shortest duration was one day; the longest, seventeen years.

TABLE V. TYPE OF BLEEDING WITH REFERENCE TO PATHOLOGIC LESION

	MALIGNANT	BENIGN	TOTAL
Rhythmical	6 (1.1%)	11 (2.1%)	17 (3.2%)
Profuse	75 (14.6%)	126 (24.4%)	201 (39%)
Spotting	78 (15.1%)	147 (28.5%)	225 (43.6%)
Bloody discharge	26 (5.5%)	45 (8.7%)	71 (14.2%)
Totals	185 (36%)	329 (64%)	514 (100%)

Summary

1. A brief review of the literature is presented.

2. A survey is made of 514 cases of genital bleeding two or more years after cessation of menstruation.

3. Criteria are reviewed with respect to: (a) pathologic findings according to location, (b) race, (c) age at menopause, (d) duration of amenorrhea before bleeding, (e) duration of bleeding, (f) type of bleeding.

4. Explanatory comments are made concerning some of the more interesting cases.

Conclusions

1. Of the 514 cases presented, 36.1 per cent had malignant lesions. This is a lower figure than that usually quoted, and reflects increasing understanding on the part of the patient of the danger of postmenopausal bleeding, better understanding and cooperation on the part of attending physicians in referring patients for study, and possibly a greater incidence of benign bleeding from hormonal stimulation.

2. No significant difference in etiology is noted when the group is divided according to race, except that cervical prolapse associated with bleeding was uncommon in the Negro race.

3. The average age of cessation of menstruation was 47.8 years. In the groups divided according to age at the menopause, there is apparently no real difference in percentage of malignancy. There is an increasing percentage of malignancy with increasing age of the patient at the time of examination.

4. There is no relation of duration of amenorrhea to the causal lesion. The average of 10.1 is higher than expected.

5. Duration of bleeding ranges from one day to seventeen years and bears no relation to pathology.

6. Type of bleeding varies from spotting to profuse hemorrhage and is found to have no significance in determining the etiology.

7. Bleeding after the menopause may come from anywhere in the genital tract. To rule out malignancy a complete study, including uterine curettage and biopsy of the cervix, is imperative in all cases regardless of findings on pelvic examination.

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LATE POSTPARTUM ECLAMPSIA*

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POSTPARTUM eclampsia occurs most frequently during the first day of the puerperium, while in only a relatively small number of cases does the attack appear on the second day after the birth of the child. It is generally stated that convulsions appearing later in the puerperium are due to such causes as hysteria, epilepsy, or uremia rather than eclampsia. A few instances have been reported in which convulsions occurred several weeks after delivery, but the evidence presented with these reports is insufficient to substantiate the diagnosis of postpartum eclampsia.

Until recently, our experience has led to the conclusion that postpartum eclampsia invariably occurs within seventy-two hours following parturition. In light of the data presented below, this belief becomes untenable and must be altered to include the first week of the puerperium.

Table I. Postpartum Eclamptics. Time of First Convulsion

HOURS FOLLOWING DELIVERY	NUMBER OF CASES	PER CENT OF TOTAL	SUM OF PERCENTAGE
0 to 6	12	50	50
6 to 12	4	17	67
12 to 24	4	17	84
24 to 30	1	4	88
Over 30	3	12	100
Total	24	100	

In the New York Lying-In Hospital, during the period from Sept. 1, 1932, to Jan. 1, 1946, we have had 70 cases of eclampsia of all types, an incidence of one in every 547 premature and full-term deliveries. Of these eclamptic patients, 24, or 34 per cent, suffered from the postpartum variety. An analysis of these (Table I) shows that the first convulsion occurred within thirty hours of delivery in 21 cases. In other words, the attack of postpartum eclampsia came on well within the seventy-two hours following parturition in 88 per cent of women suffering from this variety of the disease. There remain three cases, detailed in this paper, in which the eclamptic seizure made its appearance after this seventy-two hour period, one occurring on the fourth, one on the sixth, and one on the eighth postpartum day. A summary of the pertinent findings in these three patients follows.

Case 1.—Mrs. M., a 31-year-old primigravida, registered in the antenatal clinic in the seventeenth week of her pregnancy. Her past history was relevant in that during the preceding four years she had had episodes of hyper-

*Supported by a grant from The John and Mary R. Markle Foundation.

tension, ranging up to 168/96, associated with emotional stress. At the time of her first visit, in the present pregnancy, her blood pressure was 155/85; there was no edema and no proteinuria. During subsequent visits her blood pressure ranged from normal to borderline values without accompanying edema or proteinuria, and weight gain was within normal limits. However, one week prior to the expected date of confinement the blood pressure rose to 150/100 associated with a one plus edema. Hospital study revealed no physical abnormalities; the retinal findings and blood chemistries were normal. The hypertension and edema responded satisfactorily on bed rest, and after one week in the hospital she was discharged.

Two weeks later the patient was readmitted in labor. The blood pressure at this time was 145/80, and all other findings were otherwise normal. Delivery of a 3,570 Gm. normal female infant was spontaneous after twelve and three-fifths hours of uneventful labor. During the first six postpartum days the blood pressure was normal to borderline, with varying minimal proteinuria.

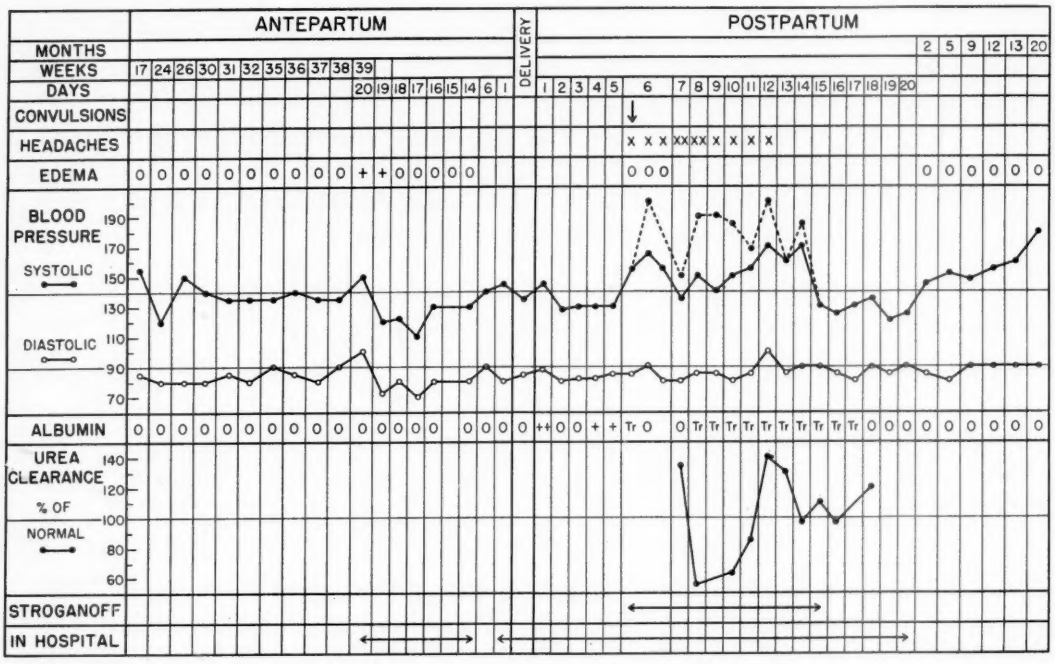

Fig. 1.—Case 1, clinical findings.*

On the morning of the sixth postpartum day the patient had a headache for the first time; this was severe and associated with blurring of vision. Blood pressure was 155/90. One hour later, with persistence of symptoms, the pressure was 180/90, and within a few minutes she was seized with generalized convulsions. She was temporarily unconscious and questionably incontinent. Blood chemistries performed at this time revealed a nonprotein nitrogen of 28.6; uric acid of 4.1 mg. per 100 c.c. of blood; and a CO_2 combining power of 25 volumes per cent. She was immediately started on a modified Stroganoff regime, and within a few hours was relieved of symptoms, the blood pressure returning to lower levels.

In the following eight days the elevated systolic blood pressure fluctuated widely, although the diastolic pressure was maintained at about 90. During the remainder of the hospital stay the blood pressure was within normal limits.

*The average systolic pressure during a given period is indicated by the solid line. The dotted lines indicate the highest recorded pressure which occurred.

Likewise, there was a gradual return to normal values in the blood chemistries. The urine output was satisfactory throughout and contained only a trace of proteins. A urea clearance test on the twentieth postpartum day showed a clearance of 116 per cent of normal. Retinoscopic examination following the convulsion was negative. A lumbar puncture on the third day following the convulsion revealed normal pressure, clear fluid, and negative microscopic findings. Protein was 75 mg. per cent. She was discharged in good condition on the twenty-first postpartum day.

The patient was followed at stated intervals in the postpartum toxemia clinic for two years and eight months. Her only complaints were occasional precordial pains. There was no proteinuria and no edema. The blood pressure, however, showed a progressive rise in systolic to 180, but with a maintenance in the diastolic at 90. Diagnosis: postpartum eclampsia in a patient with essential hypertension. Blood pressure readings, urine and blood chemical findings, and other pertinent data are portrayed in Figs. 1 and 2.

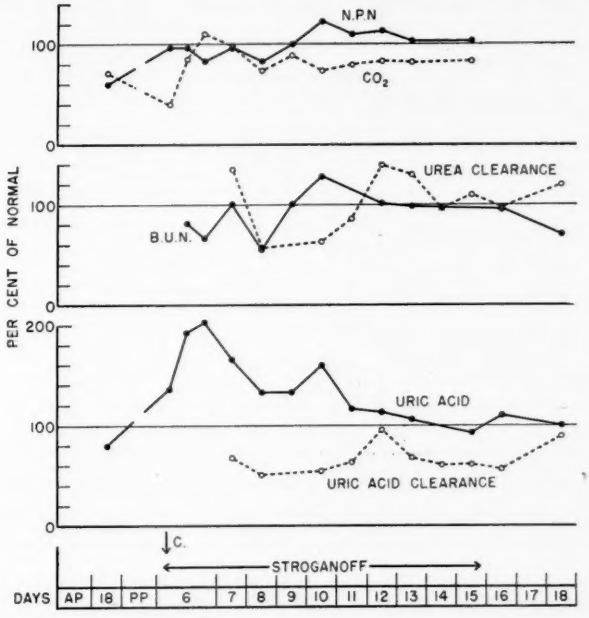

Fig. 2.—Case 1, laboratory findings in blood and urine.*

Case 2.—Mrs. T., aged 42 years, an elderly primigravida, registered in the antenatal clinic in the seventeenth week of her pregnancy. Her past history was negative. The physical examination at this time was normal, including normal blood pressure values and normal pelvic measurements. Her antepartum course was uncomplicated, except for a slight anemia, until in the thirty-second week, when a one plus proteinuria appeared associated with a four plus edema, blood pressure being normal. One week later the urine was negative for albumin, the edema was unchanged, and the blood pressure was 120/90. In the thirty-fourth week the blood pressure was 140/88. Multiple pregnancy (twins) had been recognized since the twenty-ninth week. The weight gain was normal, i.e., 8 kilograms, or 12 per cent.

The patient was admitted in premature labor in the thirty-fifth week. After an uneventful seven and one-fifth hour labor, a 2,070 Gm. living female

*Normal values (100 per cent) taken to be as follows: N. P. N. = 30 mg. %; CO_2 capacity = 65 vol. %; B. U. N. = 12.5 mg. %; Urea clearance, maximal = 75, standard = 54, 24 hour = 63 ml./min.; Blood uric acid = 3.0 mg. %; Uric acid clearance, short period = 14, 24 hour = 12.5. All clearances except the last ones are 24 hour clearances.

infant and a 2,180 Gm. living female infant were delivered by low forceps and by breech extraction, respectively. The blood pressure on admission was 155/90, but dropped to normal later in labor.

The first three days following delivery were uncomplicated. At 11:15 A.M. on the fourth postpartum day, the patient was seized with generalized convulsions, preceded by visual disturbances described as "spots before the eyes." Within six hours she had three additional convulsive attacks. She was unconscious after each attack. The blood pressure at the time of the first convulsion was 140/90, rising to 200/76 with the second seizure. The optic fundi were visualized and found normal. Blood taken at the time of the first episode revealed a uric acid of 3.9 and a CO_2 combining power of 29.6 volumes per cent. Within a few hours the uric acid had increased to 4.9, but under treatment the CO_2 combining power returned to normal. The urine contained three plus albuminuria. The patient was given sedation, and the blood pressure slowly returned to normal over the course of the next two weeks. Likewise, the blood chemical changes had returned to normal in thirteen days.

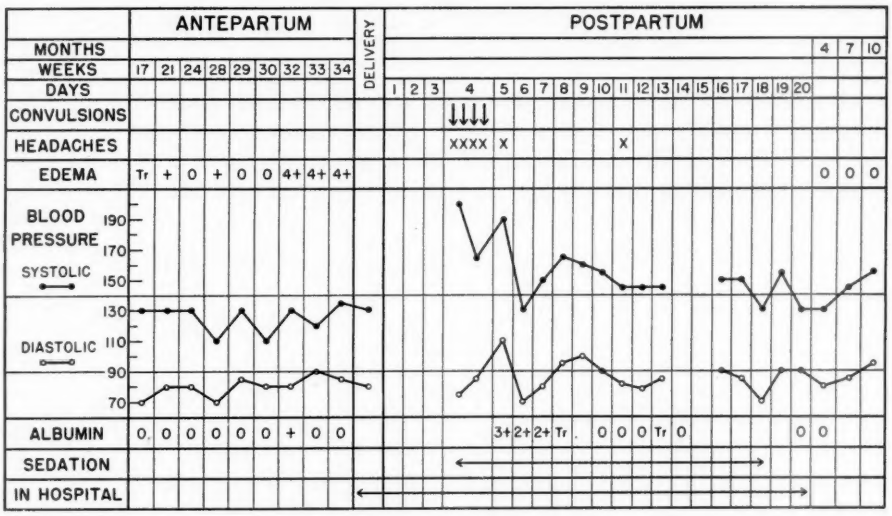

Fig. 3.—Case 2, clinical findings.

Proteinuria persisted for four days. Lumbar puncture on the day of convulsions revealed an initial pressure of 180, dropping to 120 mm. later; microscopic and chemical determinations were normal. Skull x-rays were normal. There was no past history of convulsions, save for one attack in infancy. Her course was afebrile save for a single temperature rise to 38.8° C. (rectal) following the convulsive seizures. She was discharged in good condition on the twenty-first postpartum day.

The patient was seen in the postpartum toxemia clinic at stated intervals, and was last observed ten months post partum. She had no complaints, and the only abnormal finding was a final blood pressure of 155/95, as shown in Fig. 3. Diagnosis: Postpartum eclampsia.

CASE 3.—Mrs. M., a 25-year-old white para 0, gravida ii, registered in the antenatal clinic in the eighteenth week of pregnancy. Her past history was negative. Physical examination was normal with normal blood pressure. A Wassermann test was negative, the blood was type A and Rh negative. Her antepartum course was uneventful until the beginning of the thirtieth week, when the diastolic blood pressure became elevated. Both systolic and diastolic

pressures were elevated in the thirty-second week and in the thirty-fourth week; because of a blood pressure of 145/100 associated with two plus proteinuria and two plus edema, she was admitted for hospital care. The weight gain was not excessive, i.e., 9 kilograms, or 12 per cent, and the patient had no untoward symptoms.

The admission physical examination was normal, except for the presence of moderate edema and hypertension. The fetus was thought to be viable, although premature. Fundiscopic examination was normal. Blood uric acid was elevated to 5.5 mg., with a lowered CO_2 combining power of 43.0 volumes per cent and a normal nonprotein nitrogen. Because the objective findings gradually became more pronounced, a modified Stroganoff management was started on the third day of hospitalization. Some temporary improvement resulted, although the urine output remained low, associated with an unabating proteinuria.

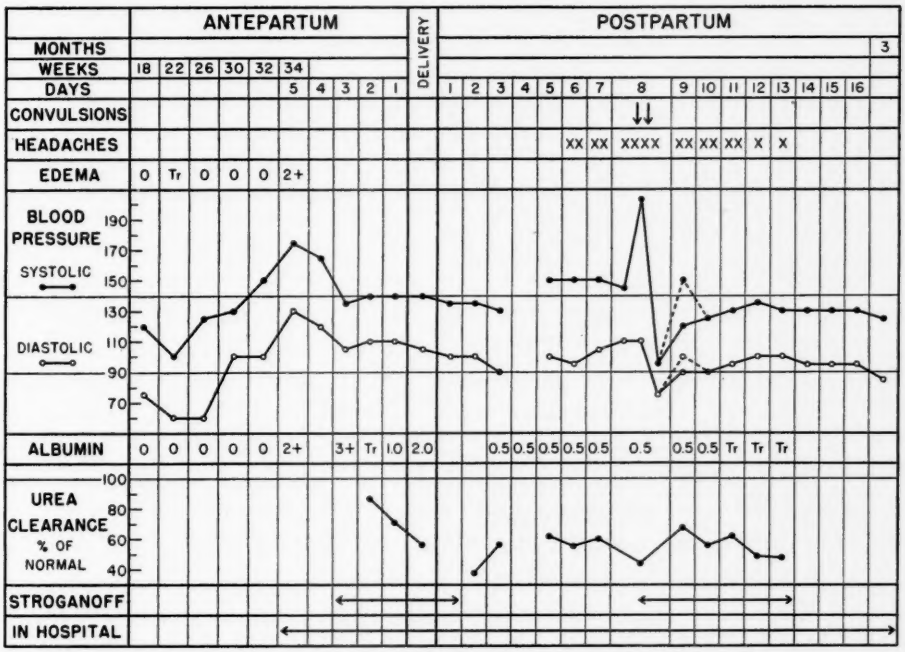

Fig. 4.—Case 3, clinical findings.*

Labor set in spontaneously three days later; shortly thereafter the fetal heart was lost. After seven and two-thirds hours, a 2,130 Gm. deadborn male infant was spontaneously delivered. Measured blood loss was 500 c.c., and this was promptly replaced by transfusion. Immediately post partum the blood pressure was 150/110 and the blood uric acid was 6.4. A fever of 38.0° C. on the day of delivery and first postpartum day was attributed to dehydration. A Stroganoff treatment was discontinued the day following delivery because of improvement in the blood pressure and proteinuria. The blood uric acid, however, remained high. The postpartum course was uneventful through the seventh day, except for the development of persistent severe headache on the sixth day.

On the morning of the eighth day she again complained of severe occipital headache, and later in the day this was associated with blurring of vision. The blood pressure was 146/110 and the morning blood specimen showed a uric

*See footnote, p. 766.

acid of 5.9, nonprotein nitrogen of 37.1, blood urea nitrogen of 16.9, and a CO_2 combining power of 51.4 volumes per cent. At 7:15 P.M. of the same day the patient had an attack of generalized convulsions associated with unconsciousness, frothing at the mouth, and sphincter incontinence. Blood pressure was 205/110. Twenty minutes later, when venipuncture was being performed, a second convulsive attack occurred. Blood taken at this time showed no essential change. Neurological examination two hours later was negative, and likewise fundiscopic examination was again normal. There had been no past history of convulsions or of epilepsy. Hence, a repeat course of modified Stroganoff therapy was started. The blood pressure responded and returned to a normal range after nine days. The blood uric acid and nonprotein nitrogen gradually returned to normal.

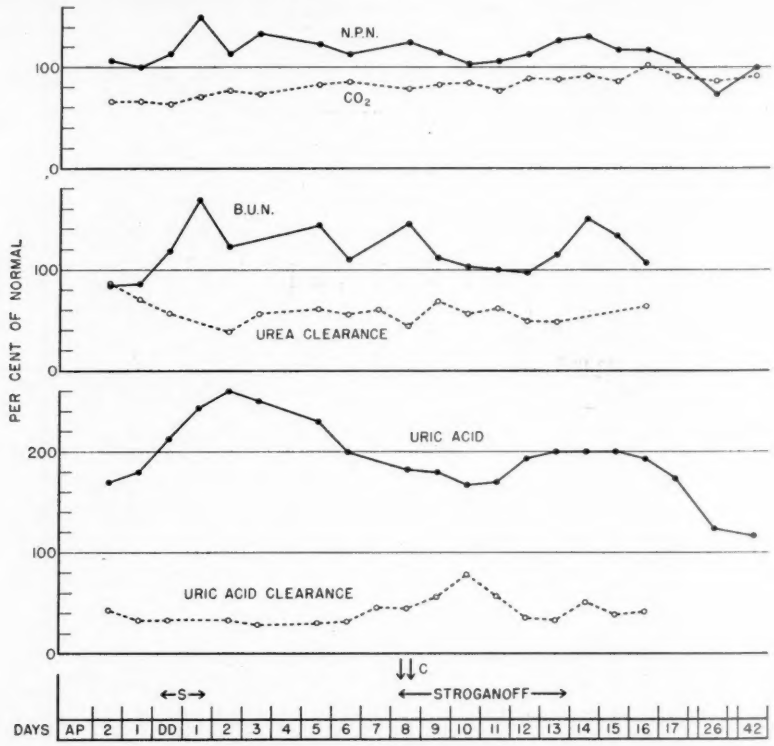

Fig. 5.—Case 3, laboratory findings.*

The postpartum course was further complicated by a right lower lobe bronchopneumonia developing on the seventeenth day. The organism was alpha prime streptococcus. This secondary infection was attributed to aspiration at the time of the convulsions. Chemotherapy and penicillin were given. Notwithstanding, lung abscess occurred. This, in turn, improved with postural drainage and conservative therapy. The patient was finally discharged in good condition on the sixty-second postpartum day. The laboratory and other findings in this case are shown in Figs. 4 and 5. Diagnosis: Postpartum eclampsia.

Discussion

Clinical Findings.—From a study of the clinical data relating to past history, blood pressure levels, water retention (edema), convulsive seizures, eye-

*See footnote, p. 767.

ground changes, urinary output, symptomatology, neurological signs, and subsequent follow-up findings in a toxemia clinic over extended periods, we feel amply justified in establishing the diagnosis of postpartum eclampsia in each of these three patients. It should be noted that in all three the outbreak of fits was preceded by signs and symptoms of "toxemia," and that in Case 1 hypertension persisted long after the disappearance of the eclampsia, while in Case 3, in which the first convulsion occurred on the eighth postpartum day, there was a return to normal, in all respects, nine days after the attack.

Laboratory Findings.—The chemical and other laboratory data, shown in the accompanying charts, are as convincing as the clinical findings, and substantiate the diagnosis of postpartum eclampsia.

In the first two cases the blood uric acid and the CO_2 combining power behaved as in eclampsia, the former rising and the latter falling to moderately low levels. However, part of the increase in the blood uric acid in the first case may have been caused by the sodium lactate which was infused. The nonprotein nitrogen and the urea levels remained essentially within normal limits in both these cases, although the first case shows a transient increase of questionable significance in the urea nitrogen, and therefore in the nonprotein nitrogen on the third and fourth days following the convulsions. A similar change in these values might possibly have occurred after the same relative time following the convulsions in the second case, but no data are available.

The blood findings in the third case are atypical, probably because this patient suffered from severe pre-eclampsia ante partum. It will be noted that there is a distinct elevation in the nonprotein nitrogen, uric acid, and urea nitrogen levels following delivery. These values then decrease slightly up to the time of the convulsive episode and are not altered markedly by it. Nor is there any particular change in the CO_2 combining power at this time. However, a rise in the nonprotein nitrogen due to an increase in the urea nitrogen appears again as in the first two cases some days following the convulsive seizure; this time on the fifth and sixth days following the episode.

Kidney function with respect to urea and uric acid was followed in these cases by the procedures described by Bonsnes and Stander.[1] In the first case the urea clearance shows a depression which is reflected in the rise in the blood urea nitrogen. The uric acid clearance is generally low except for one day, but it seems to be improved by the twelfth day following the convulsion. In the second case the urea clearance was depressed and the uric acid clearance was normal on the two occasions when such tests were carried out (the second and eleventh days following the convulsions). No other data are available. In the third case the uric acid clearances were definitely depressed throughout the period in which they were studied.

It is not possible to interpret these laboratory findings at the present time. We have pointed out in the publication cited above that these changes in the blood levels of uric acid and urea can probably be attributed in large part to an alteration in kidney function. But such an interpretation does not seem to account for the changes observed in all cases. Yet, these laboratory findings are similar to those observed previously in cases which have been classi-

fied clinically as eclampsia and severe pre-eclampsia and, therefore, in conjunction with the clinical data, support the contention that these are actual instances of late postpartum eclampsia.

A review of the total 24 patients with postpartum eclampsia reveals that one had antepartum eclampsia, five suffered from severe pre-eclampsia eventuating in postpartum eclampsia, five had antepartum "toxemia" preceding the eclampsia, while thirteen women had no antepartum pre-eclampsia or "toxemia." In other words, in more than half of the cases, the postpartum eclampsia made its appearance without signs or symptoms indicative of toxemia during the antepartum or intrapartum periods. This is most significant in that eclampsia, although always associated with gestation, may occur days after delivery of the child and placenta in a woman apparently normal up to the time of the attack. From this it would almost seem as if the causative agent of the disease must be confined to the maternal organism, although undoubtedly activated or conditioned by the product of conception.

Summary

Postpartum eclampsia may occur at any time during the first week of the puerperium. Three cases of late postpartum eclampsia are presented, one occurring on the fourth, one on the sixth, and one on the eighth day following delivery. Each of these showed most of the typical clinical and laboratory findings of eclampsia, namely, hypertension, albuminuria, edema, convulsions, elevated blood uric acid and decreased CO_2 combining power, decreased uric acid clearance and decreased urinary output, followed by a complete return to normal after the eclampsia, with the single exception of persistent hypertension in one of the three patients.

Reference

1. Bonsnes, R. W., and Stander, H. J.: J. Clin. Investigation 25: 378, 1946.

THE SELECTION OF FORCEPS FOR MIDPELVIC ARREST OF THE VERTEX

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STUDIES of the results of forceps delivery have more or less evaded statistical analysis. It has not been possible to compare the effectiveness of one instrument or one maneuver with another, for such factors as the relative skill of the operator and, even more, the range of the indications for the operation, are of enormous importance in determining the outcome. Nevertheless, midpelvic arrest of the vertex remains, perhaps, the most difficult and inaccessible problem in clinical obstetrics. An attempt to reduce this problem to terms by which statistical study and comparisons may be made is therefore indicated.

The principle to be followed in the selection of forceps for delivery of the vertex arrested or delayed in the midpelvis has produced at least two schools of thought. One has maintained that the practitioner or obstetrician should so thoroughly familiarize himself with one type of forceps that he can apply it, possibly after manual adjustment of the head, to any situation which may arise with the vertex presenting. The second school believes that no forceps is mechanically adapted to all vertex deliveries and that special types must be selected for application to particular positions of the occiput or to effect delivery through the most favorable diameters of the pelvis.

The selection of one of several instruments to meet each particular problem has been the practice on the Bellevue Hospital Obstetrical Service during recent years. Indications have not been standardized, and considerable freedom has been left to individual operators, both attending and resident physicians, to make their own choice of forceps. Nevertheless, a more or less consistent system has developed which is now generally followed.

The factors responsible for the development of this attitude toward the midforceps problem are to be found partly in the availability to members of the division of several types of forceps of radically different design and partly from the growing appreciation of pelvic architecture as a determining factor in the mechanism of labor.

The Theoretical Need of Several Types of Forceps

When, in 1934, the first cases of this report were being delivered, the Kielland forceps had already been used for many years on the service, and its value, particularly in posterior positions, was partly realized. At about this time the Barton forceps was introduced to the hospital and immediately found an important place in the control of deep transverse arrest. The theoretical

advantage of these forceps in their special field became more obvious in the successive years with the series of publications[5, 6, 24] on the mechanism of labor resulting from the x-ray studies of the pelvis.

Of most importance, so far as the Barton forceps were concerned, was the observation that the commonest position of the head during engagement was with the sagittal suture in a transverse diameter, and that a deep transverse position was a continuation of the position of engagement and not an incompletely rotated posterior.[5, 6] In small android and in flat pelves it was particularly emphasized that the transverse position had to be maintained until much greater descent had been accomplished than usual because at or above the ischial spines rotation might be opposed by the lateral aspects of the prominent sacral alae.

In the less common anthropoid or transversely contracted pelvis the x-ray taught that the head often entered the pelvis as a direct anterior or posterior occiput, and that this position, once assumed, must necessarily be maintained throughout the passage of the bony pelvis. In such cases, and in others in which there is simply a narrow interspinous diameter, rotation from a posterior to an anterior, either spontaneously or by forceps, would require the forcing of a head already fixed in the anteroposterior through a narrower transverse diameter. For these cases in which rotation in the midplane of the pelvis is difficult for definite anatomic reasons, the Kielland forceps appeared to have a definite place, either to effect delivery of the head as a persistent occiput posterior, or else by elevation of the head above the brim or by traction to a lower place to permit rotation at a more favorable level.

Finally, since many of the problems in the midpelvis still concern an anterior occiput, or else an occiput that can be manually rotated in an ample pelvis to an anterior position, a classical forceps with typical cephalic and pelvic curves was required. The forceps commonly, but not exclusively, used for this was the Haig-Ferguson, a modification of the Simpson with light fenestrated blades, short handles and a readily applied traction bar. The wide separation of the shanks in this instrument has appeared especially valuable in ensuring adequate protection of the baby's head.

The physical characteristics of these forceps and the technique of their application has been sufficiently described to require no repetition here. For the Barton forceps, reference may be made to the article of Barton, Caldwell, and Studdiford;[3] for the Kielland forceps, to the paper of Jarcho.[15] The original description of the Haig-Ferguson forceps is to be found in the Transactions of the Edinburgh Obstetrical Society.

The literature on the Kielland forceps is already immense and has been repeatedly reviewed (Greenhill;[12] Fink[11]). That the interest in this instrument continues in America is shown by several recent favorable reports (Rucker, Cosgrove,[8] Vedder[25]). Contributions on the use of the Barton forceps are, however, extremely meager, being practically limited to the article just cited and to a series of 55 cases published by Bachman in 1927.

The Material Analyzed

The material for this analysis consisted in the 701 midforceps operations occurring among 10,814 deliveries on the Obstetrical Service of Bellevue Hospital from January 1, 1934, to December 31, 1945. In considering the results obtained and some of the inconsistencies in application, it is necessary to remember that the time of the report covers the service of twelve residents who were supervised at one time or another by 20 different attendings. It may be noted also that the Bellevue Service must accept new patients and transfers from other hospitals at any time, and that only three-fourths of the cases delivered were registered in the antepartum clinic of the service or subject to study before the onset of labor.

Factors Influencing the Selection of Forceps in Individual Cases

In reviewing the midforceps of the years 1934 to 1940, it is clear that various factors influenced the selection of forceps for each case.

1. *Experience.*—With the introduction of any new instrument there will be a period of trial during which staff members are learning its use. Thereafter, it may increase in popularity or else be gradually dropped. It is to the credit of the Barton forceps that its popularity steadily increased until about over half of all midforceps cases were treated with this instrument (Table I).

2. *Position of the Occiput.*—Undoubtedly the most important point on which the selection of forceps is made on the Bellevue Service is the position of the occiput. Table II shows that among the cases with anterior positions, classical forceps have been used almost without exception. In the transverse positions, about three-fourths were delivered with the Barton, while in the posteriors, over 50 per cent were delivered with the Kiellands.

The figures in Table II become clear only when it is noted that in many instances an attempt was made manually to rotate the posterior occiput to a transverse or oblique position in order to permit the use of the Barton instead of the Kielland forceps. Attempts were sometimes made also to convert the transverse to an anterior position so that the classical forceps might be used, but the growing confidence in the Barton forceps when the sagittal suture was found in the transverse led to an acceptance of this as a favorable position for application.

The relative frequency with which the several positions of the occiput are recorded is undoubtedly somewhat influenced by the obstetrician's preference as to technique of delivery. Transverse positions have been reported previously as occurring in one-fifth to one-third of all cases.[7, 19, 20] It is interesting that on the Bellevue Service, where on account of the Barton forceps the transverse position was not considered particularly unfavorable, its incidence rose to 51 per cent, a figure approaching that found in x-ray studies.[5-6]

3. *Type of Pelvis.*—Since the Kielland and Barton forceps were used predominantly for cases in which the position was transverse or posterior, and since it has been shown that there is a tendency for these positions to persist in android and anthropoid pelves[5, 6, 24] it might be expected that these less favorable types would be commoner among the groups of cases delivered by the Barton or Kielland forceps. From a review of the 243 cases on which diagnosis was made by stereoscopic roentgenogram of the pelves, there was some evidence of this tendency (Table III). Further, if the prognosis to mother or baby is adversely affected by these pelves, one must recognize at once that the Barton and Kielland forceps were given more difficult tasks than the classical forceps. Table IV shows also that contraction of the inlet was more common in the cases in which these special forceps were applied than in those in which the classical forceps were used.

TABLE I. EVOLUTION OF ATTITUDE TOWARD SELECTION OF FORCEPS

YEAR	TOTAL	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945
Classical forceps	196	46%	41%	36%	20%	18%	24%	28%	32%	24%	6%	18%	20%
Barton forceps	371	37%	26%	36%	65%	70%	69%	60%	61%	72%	81%	56%	47%
Kielland forceps	134	17%	33%	28%	15%	12%	7%	11%	7%	4%	12%	26%	32%
Total mid-forceps	701	52	102	107	82	43	45	53	41	46	48	50	34

TABLE II. POSITION OF FETAL HEAD IN RELATION TO TYPE OF FORCEPS SELECTED. PERCENTAGE OF INSTANCES OF A GIVEN POSITION OF THE OCCIPUT DELIVERED WITH EACH TYPE OF FORCEPS

		ANTERIOR		TRANSVERSE		POSTERIOR			FACE	BROW
	TOTAL	LOA	ROA	LOT	ROT	LOP	ROP	OP		
Classical forceps	196	98%	95%	11%	6%	27%	7%	38%	25%	–
Barton forceps	371	–	–	75%	87%	29%	33%	–	25%	100%
Kielland forceps	134	2%	5%	14%	7%	44%	60%	62%	50%	–
Total mid-forceps	701	101	44	191	206	34	112	8	4	1

TABLE III. TYPES OF PELVIS IN X-RAYED CASES IN RELATION TO FORCEPS SELECTED

	TOTAL	GYNECOID				ANDROID				PLATY-PELLOID	ANTHRO-POID	
	TOTAL CASES X-RAYED	PURE TYPE	ANDROID TENDENCY	PLATY-PELLOID TENDENCY	ANTHROPOID TENDENCY	PURE TYPE	GYNECOID TENDENCY	PLATY-PELLOID TENDENCY	ANTHROPOID TENDENCY	PURE PLATY-PELLOID TYPE	PURE TYPE	GYNECOID TENDENCY
Classical forceps	50	33	2	1	5	2	3	1	0	0	2	1
Barton forceps	130	66	6	18	9	3	12	3	1	8	1	3
Kielland forceps	63	26	5	5	12	3	2	1	1	0	7	1

TABLE IV. THE LENGTH OF THE TRUE CONJUGATE IN RELATION TO FORCEPS SELECTED

ANTEROPOSTERIOR DIAMETER OF INLET IN CENTIMETERS	8 TO 8.9	9 TO 9.9	10 TO 10.9	11 AND OVER	TOTAL
Classical forceps	1	7	23	93	124
Barton forceps	10	28	48	158	244
Kielland forceps	2	8	26	56	92
Total estimated cases	13	43	97	307	460

For the anteroposterior diameter of the inlet x-ray measurements were utilized in cases so studied, and clinical estimation only in the remainder.

TABLE V. WEIGHT OF BABY IN RELATION TO FORCEPS SELECTED

	TOTAL CASES	PER CENT UNDER 7 POUNDS	PER CENT 7 TO 8 POUNDS	PER CENT 8 TO 9 POUNDS	PER CENT OVER 9 POUNDS
Classical forceps	196	34	35	23	8
Barton forceps	371	31	35	26	8
Kielland forceps	134	29	34	26	10
Total	701	31	35	26	8

4. *Size of Baby.*—Large babies were distributed about equally throughout the different groups. The Kielland forceps proved more unsuitable, the babies over 8 pounds in weight being slightly more common in the group in which it was used (Table V).

TABLE VI. MATERNAL RESULTS WITH VARIOUS TYPES OF FORCEPS

	TOTAL CASES	MATERNAL DEATHS	PERCENTAGE OF MORBIDITY	PERCENTAGE OF CASES WITH BLOOD LOSS OVER 500 C.C.	INJURIES TO THE BIRTH CANAL, ACTUAL NUMBER OF CASES			
					CERVICAL LACERATIONS	SULCUS TEARS OF VAGINA	VESICOVAGINAL FISTULAS	THIRD DEGREE LACERATIONS OF PERINEUM
Classical forceps	196	2	34.1	13.2	7	12	0	1
Barton forceps	371	2	42	13.2	38	47	3	2
Kielland forceps	134	0	49.9	18.6	10	20	0	0
Total	701	4	41.3	14.2	55	79	3	3

TABLE VII. FETAL RESULTS WITH VARIOUS TYPES OF FORCEPS

	FETAL AND NEONATAL DEATHS TOTAL			FETAL AND NEONATAL DEATHS INTRACRANIAL INJURY	
	TOTAL	NUMBER	PER CENT	NUMBER	PER CENT
Classical	196	17	8.6	7	3.5
Barton	371	28	7.5	14	3.7
Kielland	134	21	15.6	16	11.9
Total	701	66	9.4	37	5.2

Results With Different Types of Forceps

The results of the use of these forceps may be considered under the headings of maternal mortality and morbidity, injuries to the birth canal, hemorrhage, and fetal mortality (Tables VI and VII).

1. *Maternal Mortality.*—There were four maternal deaths (0.56) in the series of 701 patients, two of these having been delivered by classical forceps and two by the Barton. One of these deaths, following delivery by the classical forceps, occurred in a patient receiving an intravenous infusion of toxic gum acacia that was responsible for other deaths in the hospital at about the same time. The remaining three patients died of puerperal sepsis and, although there was no gross injury, these deaths must be ascribed to the type of delivery. The corrected maternal mortality rate for midforceps deliveries was therefore only 0.4 per cent.

2. *Maternal Morbidity.*—On the basis of the standard of morbidity followed by the Bellevue Obstetrical Service, namely, a rise to 100.4° F. on at least one occasion on two separate days post partum, 41.3 per cent of the entire series of forceps cases were morbid (Table VI). The cases delivered by classical forceps had a somewhat better record than those in the Barton and Kielland groups.

3. *Injuries to Birth Canal.*—On the basis of the statistics of Table VI, it is difficult to find points for drawing comparison between the three types of for-

ceps. Blood loss of over 500 c.c. was somewhat commoner after the use of the Kielland forceps, but there was no accompanying record of increase in vaginal lacerations. The deep and early episiotomies usually needed with the Kielland forceps offer a partial explanation. The three bladder injuries following Barton forceps are noteworthy, but all were very small, and in each instance the fistula closed spontaneously.

4. *Fetal Mortality.*—When one comes to the results for the fetus there appears a decided difference in the performance of the three instruments. The gross fetal mortality, stillborn and neonatal, for the entire group of 701 cases, was 9.4 per cent. If the fetal deaths due to causes other than intracranial injury are subtracted, the mortality apparently directly ascribable to the operation becomes 5.2 per cent.

The uncorrected mortality for the three instruments was found to be the following: for the classical forceps, 8.6 per cent; for the Barton, 7.5 per cent; and for the Kielland, 15.6 per cent. When only fetal deaths due to the operation are considered, the contrast becomes still more striking, for then the mortality for the classical forceps and the Barton is only 3.5 per cent and 3.7 per cent, respectively, while that for the Kielland was about three times as high, namely, 11.9 per cent (Table VII).

This difference deserves immediate comment. In partial extenuation of the record for the Kielland, it may be noted that a greater proportion of posteriors were delivered by this instrument than by any other and, further, that in 5 of 16 deaths ascribed to the Kielland forceps other instruments had been applied without success. On the other hand, many posteriors, as well as the great majority of transversely arrested heads, were delivered by the Barton forceps with strikingly good infant results. The low incidence of intracranial injury with these forceps is probably to be ascribed in part to the possibility of perfect cephalic application to the transversely placed head, and further to the fact that rotation is accomplished deep in the pelvis where bony opposition is at a minimum.

5. *Failure of Forceps.*—In the classification of the 701 patients, each case was assigned to the forceps which had accomplished the principal part of the delivery. Actually, in 99 of these patients more than one type of forceps was employed (Table VIII). Usually the second forceps was applied to complete

TABLE VIII. USE OF MORE THAN ONE INSTRUMENT TO EFFECT DELIVERY

TYPE OF FORCEPS FIRST APPLIED		TYPE OF FORCEPS WITH WHICH DELIVERY WAS COMPLETED		
		CLASSICAL TOTAL CASES	BARTON TOTAL CASES	KIELLAND TOTAL CASES
Classical	211	183	24	4
Barton	357	30	314	13
Kielland	132	18	9	104

delivery after the first instrument had accomplished its purpose of rotation, but in about a third the second instrument was used after admitted failure of the first.

Classical forceps were first applied in 211 cases and were used to complete delivery in 183 of these. The 29 cases remaining were handled in 24 instances by the Barton, in four by the Kielland, and in one by version and extraction. These cases represent, in almost all instances, failures with the classical forceps.

The Barton forceps were the first instrument applied in 314 cases. In 21 cases, after successful rotation on the pelvic floor, the Barton forceps were replaced and delivery completed by a classical forceps as a method of choice,

but not of necessity. In the others Barton forceps were admitted failures, delivery being accomplished by one of the other instruments.

The Kielland forceps were used to complete 104 of the deliveries in which it was the original instrument applied. After successful rotation of the head to an anterior or transverse position the Kielland was removed and, in 17 instances, delivery was accomplished by classical, and in eight by the Barton forceps. In two instances the Kielland failed not only to effect delivery but also failed in rotation.

The Present Bellevue Technique

The present plan of handling midpelvic arrest on the Bellevue service, as developed from the experience just analyzed, may be outlined as follows:

With the occiput in an anterior position, the classical forceps, usually of the Haig-Ferguson type, are employed. If the occiput has successfully reached this position it can usually be assumed that descent in the transverse is no longer necessary.

With the occiput in the transverse, it is felt that this diameter is usually the best for further descent, although with a gynecoid pelvis attempts to rotate manually to an oblique position may be undertaken. If rotation is easily accomplished manually, the classical forceps are employed; otherwise descent is accomplished with the Barton forceps. In cases with an android or flat pelvis, on the other hand, and especially with forward displacement of the sacrum, manual rotation may be impossible, and continued descent in the transverse with the aid of the Barton forceps is particularly desirable. If the Barton forceps are used, rotation is carried out when crowning first occurs, and delivery can be completed with this instrument, if desired.

In posterior position, rotation, either manual or with the forceps, may be attempted in the anthropoid or transversely contracted type of pelvis, but sometimes fails. Under these circumstances the Kielland has been the instrument of choice. Whereas, in the early part of the period reported, upward displacement of the head with its rotation above the pelvic brim was frequently resorted to; this technique has recently been used with decreasing frequency. The present procedure of choice is an attempt at rotation in the midpelvis if the type of pelvis is favorable. Otherwise traction is made with the occiput still posterior, and delivery carried out with the vertex in that position or after rotation on the pelvic floor.

Discussion of Results

The importance of the midforceps problem can be best seen from a glance at the contribution of this procedure to the maternal and fetal mortality on the Bellevue Obstetrical Service. From June 1, 1934, to May 31, 1941, there were 40 maternal deaths, a rate of 3.7 per thousand deliveries. The fact that only four of these occurred in patients delivered by midforceps indicates that this procedure did not add greatly to the total maternal mortality.

During the years noted, there was a total of 227 deaths of term infants or stillbirths and neonatal death rate in this group of 2.48 per cent. Among the midforceps cases there were 41 deaths, stillborn and neonatal, among the 465 infants weighing over 5 pounds. This rate of 8.8 per cent indicates that midforceps delivery does materially increase the risk run by the term infant.

For contrast, it is interesting to consider the mortality among babies delivered by cesarean section. During the period under consideration there were

30 infant deaths among 222 deliveries by hysterotomy, or 13.5 per cent. Analysis of these deaths showed, however, that 12 were from abdominal deliveries carried out for the termination of pregnancy before the period of viability, that 10 were in cases of premature separation, two in rupture of the uterus, and one in placenta previa, and that one followed a postmortem section, and one was in a baby with congenital anomalies incompatible with life. There were only three deaths possibly attributable to the method of delivery, one being the baby of a tuberculous mother, and two being born after over fifteen hours of labor. There were no deaths of term babies in uncomplicated pregnancies delivered by elective section.

The complicated character of the problem of dystocia leading to midpelvic arrest is manifest in the variety of plans adopted by different obstetric services in attempting to solve it. The most important variables that are being tested in this way are (1) the frequency of cesarean section; (2) the conduct of the second stage, in particular with respect to its length; and (3) the technique of forceps application. Difference in attitude toward the first two of these will greatly affect forceps incidence and forceps difficulty and make it almost impossible to compare the relative value of different types of instruments and techniques of application on any statistical basis.

1. *The Cesarean Section Rate.*—A high incidence of cesarean section will be accompanied by a decreased frequency of forceps delivery and improved figures for that procedure, since it will in general be the difficult cases of borderline pelvis, large babies, malposition and "cervical dystocia" that are transferred to the cesarean section column. A low incidence of cesarean section might be expected to increase the burden placed on the forceps and would probably raise both the total and the percentage of bad results from this instrument.

2. *Attitude Toward Proper Length of Second Stage.*—If only a short second stage is permitted before operative delivery is resorted to, forceps will frequently be applied, but the percentage of bad results should be low, since many relatively easy cases will fall in the forceps column. On the other hand, if the policy is followed of supporting a patient, a long second stage and of giving small doses of pituitrin in selected cases, the use of forceps in the midpelvis may be reduced almost to the vanishing point (Eastman). The few forceps deliveries which remain to be done, however, will be only the more difficult and the percentage, although not the total, of poor results may be high.

3. *Technique of Forceps Application and Delivery.*—The selection of one or another of the many types of instruments, the employment of manual correction of position, the level at which rotation is carried out, and a list of other technical points may also have some bearing on the results.

Search of the literature for guidance on these three particular factors yields no authoritative information. Maternal deaths from the forceps operation alone are actually so infrequent that comparisons on this basis are not very useful. In reports published since 1930, figures showing stillbirth and neonatal death rates following forceps deliveries have ranged from practically nothing to 20 per cent. Infant deaths following midforceps, based on all operation and not selected groups, have been reported with the following frequency: 2.3 per cent, Kane and Parker[16]; 5.0 per cent, Potter and Adair[21]; 5.4 per cent, Acken[1]; 6.4 per cent, Erbloh[9]; and 6.8 per cent, Hoffstrom.[13] Series of cases in which no distinction was made between applications at different

levels have sometimes shown higher figures, such as 10.0 per cent (Stander[23]); 13.6 per cent (Puppel[22]) and 20.08 per cent (Novey[18]). Since, however, the exact conditions under which these operations were carried out are rarely stated by the authors of the reports, it is not possible to tell what special factors are placed in contrast by the observed differences in results.

The basic conditions under which the midforceps operation has been performed at Bellevue since 1934 are as follows: (1) The cesarean section rate is fairly low, varying from 1.8 to 4.3 per cent (Table IX). (2) In the absence

TABLE IX. FREQUENCY OF MIDFORCEPS IN RELATION TO OTHER OBSTETRIC OPERATIONS

	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945
Total delivered patients	1691	1710	1510	1462	1459	1535	1447	1496	1625	1411	1353	1461
Percentage of operative deliveries	11.6	15.3	19.2	16.0	14.6	13.1	13.8	13.6	12.5	15.7	13.9	14.1
Percentage of cesarean sections	2.6	2.5	2.8	2.8	2.2	1.8	1.9	2.2	2.38	2.7	2.4	4.3
Percentage of high forceps	0.53	0.17	0.06	0.34	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Percentage of low forceps	3.7	5.0	7.3	5.9	17.9	6.9	7.3	8.0	7.1	8.3	6.7	6.8
Percentage of midforceps	3.1	5.6	7.0	5.6	2.9	2.8	3.8	2.7	2.2	3.4	3.7	2.1

TABLE X. FETAL DEATHS IN CASES DELIVERED BY MIDFORCEPS BY YEARS

	1934	1935	1936	1937	1938	1939	1940	1941	1942	1943	1944	1945
Classical:												
Total cases	30	45	43	20	11	11	16	13	11	3	9	7
Deaths	5	6	3	0	0	1	4	2	1	1	0	0
Barton:												
Total cases	13	25	39	50	30	28	31	25	33	39	28	15
Deaths	2	0	2	7	2	3	1	4	2	3	3	1
Kielland:												
Total cases	9	32	25	12	5	3	6	3	2	6	13	11
Deaths	5	6	0	3	1	1	0	0	0	0	1	1
Total												
All cases	52	102	117	72	46	42	53	41	46	48	50	34
Deaths	12	12	5	10	3	5	5	6	3	4	4	2

of progress a second stage of one hour in multigravida and two hours in primigravida before intervention is the rule in otherwise normal cases, but this period may be prolonged if mother and infant are in good condition. (3) The forceps technique has been based, as outlined, on the selection of one of several instruments believed to be especially adapted to the individual pelvis and the particular position of the vertex encountered. Under these conditions the midforceps operation on the Service resulted in a total stillbirth and neonatal death rate of 9.4 per cent. The deaths due to intracranial injury, that is to say, those directly attributable to the forceps operation, amounted to 5.2 per cent.

Summary and Conclusions

1. Report is made of 701 midforceps deliveries carried out on the basis of the general principle that a given type of pelvis and a given position of the vertex may indicate the selection of a special type of instrument.

2. In this series the Barton forceps was used in 371 instances, the Kielland in 134, and some form of classical instrument in 196. The gross infant mortality for the entire series was 9.4 per cent, the death rate for the Kielland delivered babies being higher than for those handled by the other types.

3. The results of forceps deliveries cannot be examined as isolated figures, but only in relation to the conditions under which they were performed. Reports published in the literature show an infant mortality from forceps ranging from 2.3 to 20.0 per cent, but such reports have usually failed to state underlying conditions and cannot, therefore, be used to demonstrate the relative merits of different techniques.

4. The problem of handling cases of actual or potential arrest in the midpelvis is evidently to be solved as much by studying the effects of varying the incidence of cesarean section or the management of the second stage as by improving the special technique employed in the forceps operation.

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COMPOSITION OF THE HUMAN PLACENTA

III. Vitamin Content

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IN THE last decade much information has been published concerning the vitamin content of the human placenta, with special emphasis on the ability of the organ to store nutriments and to bar their passage to the fetus. From these reports it seems that the placenta stores ascorbic acid quite readily, likewise vitamin D, while thiamine is absorbed to a lesser extent, and vitamin A and carotene only in very small quantities. The placenta seems to serve as a regulatory device for some of the vitamins, letting only required amounts pass to the fetus. Data on the niacin, pantothenic acid, and biotin contents of human placenta have not been published in the available literature. In the present study thiamine, riboflavin, pantothenic acid, niacin, and biotin have been determined in nine human placentas.* The collection and preparation of the material have been described in a preceding paper.[1]

Although the general microbiological procedures used in the analysis of human milk have been described,[2-4] the dried placenta required somewhat different preparation for pantothenic acid and biotin assays. (For niacin, the placenta samples were autoclaved with 0.1 *N* HCl as were the milk samples, since alkali or stronger acids did not increase the values obtained. There is, therefore, no "precursor" of niacin in placental tissue.) In determining pantothenic acid, the placentas were incubated with mylase P at pH 4.6 for forty hours at 37° C. With water extraction alone the values were 15 to 30 per cent lower. The "loosely bound" and the "firmly bound" biotin values were obtained after autoclaving with 0.1 *N* HCl for one-half hour, and 2 *N* HCl for three hours, respectively. Stronger acids or longer periods of autoclaving did not increase the biotin values.

Thiamine

The total amount of thiamine per placenta averaged 256 micrograms, of which 84 μg. was free thiamine and 172 μg. was bound thiamine (Table I).

The average amount of total thiamine per 100 Gm. of placental tissue was 47 μg. within a range of 25 to 64 μg. per 100 Gm. Neuweiler,[5] using Ritsert's thiochrome method, found lower values than this, his average for 14 mature placentas being 5.9 μg. per 100 Gm., with a range of 2.7 to 10 μg. Gaehtgen's[6] values for placental thiamine are similar to those of Neuweiler, but Dubrauszky and Lajos,[7] using Willstadt's colorimetric method, reported values ranging from 108 to 980 μg. per 100 Gm. for 25 mature placentas averaging 370 μg. These high values approach those obtained by Neuweiler after injecting the mother with thiamine, and he ascribed the high results of Dubrauszky and Lajos to either a better nutritional state of their subjects or to the use of a different method of analysis, or possibly to a combination of both.

*The investigation of the composition of the placenta was a part of studies of mothers during pregnancy and lactation, the composition of their milk, and the growth of their infants. Partial support for the investigation was given by the Nutrition Foundation, Inc.

TABLE 1. B VITAMINS

SUBJECT	WEIGHT FRESH GM.	WEIGHT DRY GM.	TOTAL THIAMINE TOTAL μG.	TOTAL THIAMINE PER 100 GRAMS FRESH WEIGHT μG.	TOTAL THIAMINE PER GRAM DRY WEIGHT μG.	FREE THIAMINE TOTAL μG.	FREE THIAMINE PER 100 GRAMS FRESH WEIGHT μG.	FREE THIAMINE PER GRAM DRY WEIGHT μG.	TOTAL RIBOFLAVIN TOTAL μG.	TOTAL RIBOFLAVIN PER 100 GRAMS FRESH WEIGHT μG.	TOTAL RIBOFLAVIN PER GRAM DRY WEIGHT μG.	FREE RIB TOTAL μG.	FREE RIB PER 100 GRAMS FRESH WEIGHT μG.
L. F.	661	96	381	58	4.0	131	20	1.4	1,480	224	15.4	311	47
V. G.	453	70	187	41	2.7	72	16	1.0	792	175	11.4	212	47
V. K.	327	45	193	59	4.3	44	13	1.0	583	178	12.9	168	51
V. L.	414	58	222	54	3.8	64	15	1.1	697	168	12.0	265	64
J. M.	592	90	382	64	4.2	105	18	1.2	958	162	10.6	261	44
D. M.	998	64	252	25	3.9	104	10	1.6	613	61	9.5	303	30
C. O.	713	58	197	28	3.4	47	6	0.8	626	88	10.7	211	30
V. S.	444	68	264	59	3.9	80	18	1.2	759	171	11.1	371	84
A. S.	642	96	231	36	2.4	112	17	1.2	869	135	9.0	566	88
Average	583	72	256	47	3.6	84	15	1.2	820	151	11.4	296	54

The average value for free thiamine in the placenta was 15 μg. per 100 Gm. of wet tissue, varying from 6 to 20 μg. (Table I). The bound thiamine varied from 15 to 46 μg. averaging 32 μg. per 100 Gm., or 68 per cent of the total. The ratio of free to bound thiamine was 1 to 2.1.

After determining the free and bound thiamine in retroplacental blood Neuweiler[8] obtained a ratio of 1 to 3.5. He also found that free thiamine in the mother's blood decreased from 5.1 at the beginning of labor to 3.2 μg. per 100 Gm. at delivery, but found no change in bound thiamine, which averaged 11.3 and 11.6 μg. per 100 Gm. at the beginning and end of labor, respectively. The retroplacental blood contained approximately the amounts of thiamine in the mother's blood after the birth of the child, 3.4 μg. of free and 11.8 μg. of bound thiamine per 100 Gm. He ascribes this decrease in the mother's blood thiamine and the low value for the retroplacental blood to several reasons: first, and chiefly, to the increased synthesis of acetyl choline, with which the placenta is richly supplied and which is one of the factors initiating muscular contractions in the birth process; second, to the changes in the energy system; and finally, to an increased transmission of free thiamine through the placenta during the process of birth, for as a result of the muscular contractions the amount of blood collecting in the uterus is very large and the fetus is better supplied with oxygen. It is logical that other substances, such as thiamine, pass the placental barrier in increased amounts. Since, according to Neuweiler, only free thiamine is transmitted to the fetus and the bound is not, it is understandable that only free thiamine decreases in the mother's blood and the level of the bound fraction remains unchanged. The lower concentration in the retroplacental blood is in striking contrast to the higher concentration of ascorbic acid found by Neuweiler. He states that this difference between thiamine and ascorbic acid reflects the fact that the placenta stores ascorbic acid, but under normal conditions does not store thiamine to the same extent. The higher ascorbic acid concentration in the retroplacental blood depends, therefore, in his belief, on the output of ascorbic acid stored in the placenta.

In his earlier article Neuweiler[5] noted that the venous cord blood had a higher content of thiamine than the arterial blood, which he concluded was the result of absorption from the placenta. Also, after injecting thiamine into the mother before the child's birth, he noted an increase of thiamine in the placenta. From these results he thought that the placenta might possess some ability to store thiamine, to guarantee the fetus a supply independent of fluctuations in the maternal diet, and affording protection from an excess of thiamine which might exert an unfavorable influence on sugar metabolism. In his later work[8] he states that the placenta evidently does not store thiamine as

IN HUMAN PLACENTA

OFLAVIN	NIACIN			PANTOTHENIC ACID			BIOTIN, FIRMLY BOUND			BIOTIN, LOOSELY BOUND		
PER GRAM DRY		PER 100 GRAMS FRESH	PER GRAM DRY		PER 100 GRAMS FRESH	PER GRAMS DRY		PER 100 GRAMS FRESH	PER GRAM DRY		PER 100 GRAMS FRESH	PER GRAM DRY
WEIGHT μG.	TOTAL MG.	WEIGHT MG.	WEIGHT MG.	TOTAL μG.	WEIGHT μG.	WEIGHT μG.	TOTAL μG.	WEIGHT μG.	WEIGHT μG.	TOTAL μG.	WEIGHT μG.	WEIGHT μG.
3.2	17.43	2.64	0.18	3043	460	31.6	16.5	2.5	0.17	4.2	0.6	0.04
3.0	9.90	2.18	0.14	1206	266	17.3	8.7	1.9	0.12	1.4	0.3	0.02
3.7	7.64	2.34	0.17	854	261	18.9	5.4	1.6	0.12	1.6	0.5	0.03
4.6	9.25	2.23	0.16	1443	348	24.8	7.6	1.8	0.13	1.6	0.4	0.03
2.9	13.05	2.20	0.14	1899	321	21.1	10.8	1.8	0.12	1.8	0.3	0.02
4.7	9.00	0.90	0.14	1061	106	16.5	6.9	0.7	0.11	1.2	0.1	0.02
3.6	7.88	1.10	0.14	964	135	16.5	6.1	0.8	0.10	1.5	0.2	0.03
5.4	11.03	2.48	0.16	1403	316	20.6	8.6	1.9	0.13	1.8	0.4	0.03
5.9	11.90	1.85	0.12	1939	302	20.2	9.8	1.5	0.10	2.8	0.4	0.03
4.1	10.79	1.99	0.15	1535	279	20.8	8.9	1.6	0.12	2.0	0.4	0.03

readily as it does ascorbic acid, but rather acts as an active barrier regulating the amounts of thiamine that pass through to the fetus.

The studies of Neuweiler[9] on the excretion of thiamine in the urine of newborn infants indicated that only small amounts are emitted in the first few days of life.* Oral administration of thiamine by Neuweiler produced immediate excretion from the kidneys, indicative of good absorption, but giving the mother large doses of thiamine before delivery did not appreciably increase urinary excretion of this vitamin by the newborn, the placenta evidently having served as a barrier.

The total thiamine in placenta averaged 47 μg. per 100 Gm. of fresh tissue, an amount similar to those found by Taylor, Pollack, and Williams[10] in the stomach, testes, skin, ileum, mammary glands, ovary, and seminal ducts, but lower than were found in the heart, liver, kidney, brain, lung, spleen, and muscle. The value of 3.6 μg. per Gm. of dried material (Table I) resembles the amounts in the same tissues and also those in the adrenals and colon. Placenta contains only one-fourth to one-fifth of the amounts of thiamine in the heart and kidney, which average 18 and 14 μg. per Gm. of total solids, respectively.[10]

Riboflavin

Total riboflavin per placenta averaged 820 μg. ranging from 583 to 1,480 μg. The free fraction of riboflavin averaged 296 μg. per placenta. Per 100 Gm. of fresh tissue, the averages were 151 μg. of total riboflavin and 54 μg. of free riboflavin (Table I).

Neuweiler's[11] total riboflavin values for seven mature placentas averaged 316 μg. per 100 Gm., within a range of 150 to 540 μg., and from the wide variations found in placentas examined at different stages of development he concluded that the riboflavin supply of the fetus is decidedly variable. He believed that since the passage of riboflavin to the fetal organism through the placenta is assumed to be dependent upon the endocrine glands, which develop markedly during pregnancy, the variation in the supply of riboflavin to the fetus might explain the avitaminotic condition observed in newborn infants. Neuweiler found the larger part of the riboflavin to be in the bound form (35 to 54 per cent) and he questioned whether the large amount of the bound fraction indicates a storage capacity of the placenta for riboflavin.

In this study, bound riboflavin averaged 64 per cent of the total riboflavin. The values per 100 Gm. of fresh placental tissue (Table I) approximate those obtained by Taylor, Pollack and Williams[10] for colon, testes, brain,

*The excretion of vitamins and minerals in the urine of the infants and the mineral composition of the placentas will be reported in subsequent publications.

lung, muscle, skin, mammary gland, and seminal ducts, but are lower than their values for heart, liver, kidney, spleen, adrenals, stomach, ileum, and ovary. On a dry weight basis, the placenta values exceed the amounts reported[10] for skin, mammary gland, and seminal ducts, but compare well with the values for colon, testes, brain, lung, and muscle.

Niacin

In the nine placentas the amounts of niacin ranged from 7.64 to 17.43 mg., averaging 10.79 mg. per placenta (Table I). The placenta tissue averaged 151 μg. per Gm. of dry material, a value almost as high as those published for liver and kidney,[10] 202 and 196 μg. per Gm. dry weight, respectively, and similar to those for muscle and heart tissues.

The placenta contained 1.99 mg. of niacin per 100 Gm. of fresh tissue, an amount equal to or greater than the amounts found in other tissues by Taylor, Pollack, and Williams,[10] with the exception of heart, liver, kidney, and muscle.

Pantothenic Acid

The average amount of pantothenic acid per placenta was 1,535 μg., within a range of 854 to 3,043 μg. (Table I). Per gram of dry material the average, 20.8 μg., is higher than values which have been found[10] for skin, muscle, mammary gland, and seminal ducts, and approximates the amounts found in spleen, adrenal glands, ovary, stomach, ileum, and lung. The contents reported for heart, liver, kidney, brain, colon, and testes far exceed the amount in placenta tissue.

On a wet weight basis the pantothenic acid content of placenta, 279 μg. per 100 Gm., is lower than the amounts in all the tissues analyzed by Taylor, Pollack, and Williams,[10] except skin, seminal ducts, ovary, and mammary gland.

Biotin

The total amount of firmly bound biotin per placenta averaged 8.9 μg., ranging from 5.4 to 16.5 (Table I). The loosely bound* fraction was about one-fourth of the total biotin. The dry placenta tissue contained 0.12 μg. of firmly bound biotin per gram, an amount higher than that reported by Taylor, Pollack, and Williams[10] for skin and approximating their values for lung, muscle, ovary, and seminal ducts. It is much lower than their values for tissues such as liver or kidney, which averaged 2.4 and 3.5 mmg. per Gm., respectively.

TABLE II. RELATIONSHIPS BETWEEN VITAMIN CONTENTS AND HEAT OF COMBUSTION OF HUMAN PLACENTA

	THIAMINE		RIBOFLAVIN	NIACIN	RATIO	
SUBJECT	PER 1000 CALORIES MG.	PER 1000 CALORIES NOT FAT MG.	PER 1000 CALORIES MG.	PER 1000 CALORIES MG.	THIAMINE TO RIBOFLAVIN	THIAMINE TO NIACIN
L.F.	0.75	0.81	2.90	34.2	0.26	0.022
V.G.	0.54	0.58	2.30	28.7	0.24	0.019
V.K.	0.81	0.88	2.46	32.2	0.33	0.025
V.L.	0.72	0.78	2.28	30.2	0.32	0.024
J.M.	0.86	0.94	2.16	29.4	0.40	0.029
D.M.	0.74	0.79	1.79	26.3	0.41	0.028
C.O.	0.64	0.68	2.02	25.5	0.32	0.025
V.S.	0.73	0.79	2.10	30.5	0.35	0.024
A.S.	0.51	0.54	1.93	26.4	0.27	0.019
Average	0.70	0.75	2.23	29.3	0.31	0.024

*The loosely bound was determined by autoclaving 30 minutes with 0.1 normal hydrochloric acid, while the firmly bound was released by autoclaving 3 hours with 2 normal hydrochloric acid.

Discussion

In comparison with values reported by Taylor, Pollack, and Williams for other tissues, niacin is the only one of the B vitamins considered here which is present in relatively large amounts.

Some relationships of the B vitamins in the placenta to each other and to the energy value are shown in Table II. Thiamine per 1,000 calories averaged 0.7 mg., which is more than was found in diets shown to be adequate for lactating women.[12] However, on the basis of calories not fat they are quite similar, that of placenta being 0.75 mg., while the diet contained 0.8 mg. per 1,000 calories.[13] The ratio of thiamine to riboflavin in placenta was 0.31; that of the diets of lactating women, 0.39. In studies[12] on human milk the thiamine to riboflavin ratio was found to be 0.36.[3, 4] In comparing the ratio in placenta with ratios calculated from values in the literature[10] for human tissues, similarity was found to those for heart, testes, and skin. In placenta, riboflavin averaged 2.2 mmg. per 1,000 calories, which is greater than the amount found in the diets of lactating women, 1.07 mmg.[12]

The ratio of thiamine to niacin in placenta was 0.02 to 1, which is much lower than that for the diet of lactating women, 0.07 to 1,[12] or that of human milk, 0.08 to 1.[2, 3] The ratio in placenta is lower than that in any of the tissues reported,[10] but approaches those for muscle, stomach, and ovary. In the ratios for thiamine to riboflavin and for thiamine to niacin, the placenta does not resemble closely any other human tissue for which values have been reported.

Summary

For nine human placentas the average fresh weight was 583 Gm., the dry weight was 72 Gm. The average content of total thiamine was 256 migrograms; of free thiamine, 84 mmg.; total riboflavin, 820 mmg.; free riboflavin, 296 mmg.; niacin, 1.99 mg.; pantothenic acid, 1,535 mmg.; firmly bound biotin, 8.9 mmg.; and of loosely bound biotin, 2.0 mmg. Per 100 Gm. of fresh weight the average content was: total thiamine, 47 mmg.; free thiamine 15 mmg.; total riboflavin, 151 mg.; free riboflavin, 54 mmg.; niacin, 1.99 mg.; pantothenic acid, 279 mmg.; firmly bound biotin, 1.6 mmg.; and loosely bound biotin, 0.4 mmg.

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PRESENT STATUS OF TRANSFUSION OF WHOLE BLOOD AND ITS DERIVATIVES IN OBSTETRICS AND GYNECOLOGY*

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THE therapeutic value of blood transfusions is well recognized by obstetricians and gynecologists. Sudden and alarming hemorrhage is frequently encountered by them. In his analyses of maternal deaths in Brooklyn, Gordon[1] found that hemorrhage has been the most frequent, and so the most important cause of maternal deaths for the past ten years. In view of these facts and of recent technical advances in the field of blood therapy, and because of certain safeguards that are peculiarly essential for transfusing women potentially capable of pregnancy, a review of the status of blood transfusion as it concerns obstetrics and gynecology seems important at this time.

A decade ago blood transfusion was considered a major surgical procedure. Today, transfusions are routinely given by the house staff. It is conceded that with modern methods the actual transfusion of blood requires little training, particularly since indirect transfusions are the procedure of choice. Nevertheless, the selection of the proper blood to be administered to a particular patient requires considerable knowledge. Such responsibility cannot be delegated entirely to the laboratory, but must be borne by the attending physician also. This entails knowledge of the proper method for the collection, preservation, and administration of blood, as well as various tests for blood groupings, Rh factor, and crossmatching, and the awareness that the transfusion of some blood or plasma may result in antibody formation causing subsequent difficulties.

As a result of the tremendous experience gained during the recent war, the closed system vacuum technique for the collection, storage, and administration of whole blood is recognized as the ideal and safest method for transfusions.[2] Blood is drawn, stored, and dispensed in vacuum bottles. The technique is as simple and foolproof as present-day knowledge can insure. The vacuum technique practically assures absence of bacterial contamination and, if the tubing and needles used are properly cleaned, the occurrence of pyrogenic reactions can be reduced to a minimum. Until recently, 4 per cent sodium citrate solution has been used as the anticoagulant and preservative for the usual indirect transfusion. Blood stored in this medium is satisfactory for use for about five to seven days. Since in the future "bank" blood will largely be used, a preserving solution of longer effectiveness is required. Of the various solutions available at present, ACD solution, which is a mixture of citric acid, sodium citrate, and dextrose, is the most satisfactory. This solution will adequately preserve whole blood, when stored at 4° C., for twenty-one days after collection.

The recognition that proper replacement of blood loss by whole blood is essential in the therapy of hemorrhage renders inadequate most of the present-

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day methods of procuring blood donations. It is estimated conservatively that four pints of blood per bed per year are required to meet minimum transfusion demands.[3] Unofficial surveys indicate that few, if any, of the hospitals in the United States can constantly maintain an adequate supply. Hospital blood banks, which usually exist through the solicitation of donors by the patient and the physician, are finding it difficult, if not impossible, to meet their needs. Recently, the American Red Cross, as a result of experience with its plasma and whole blood program, has announced its willingness to participate with the medical profession in a community project for the procurement of blood. This comprehensive plan calls for a community blood bank in the cities and larger towns to supply all hospitals in the vicinity with blood at no cost to the hospital or patient. In smaller communities with one or two hospitals, the Red Cross will act as a procurement agency for the hospital blood bank under the same no cost policy. These plans are actually in operation in a few localities, and need only the request and support of the medical profession for their establishment elsewhere. Thus, all blood procurement problems should be solved completely and satisfactorily.

Indications for the transfusion of blood are well accepted. Briefly, it may be stated that cases of hemorrhage and shock associated with hemorrhage should be treated with whole blood. Shock not accompanied by blood loss should have plasma infusion. Patients with anemia may be treated with whole blood or with red cell suspensions.

The proper transfusion of whole blood requires the administration of not only group compatible, but also Rh compatible blood. Of paramount importance to the obstetrician and gynecologist is the fact that whenever a transfusion is given to a woman potentially capable of childbearing, a double responsibility rests on the physician. He must be certain to give blood that will cause no immediate reaction. He must also take care not to stimulate isoantibody formation which may result in future difficulties for the pregnant woman and her fetus.

The role played by the Rh factor in the etiology of congenital hemolytic anemia and of transfusion reactions is well known.[4, 5] Rh-negative women may become sensitized to the Rh factor and develop Rh antibodies in two ways. They may develop these antibodies as the result of carrying an Rh-positive child, or they may have been transfused with Rh-positive blood, causing the subsequent formation of Rh antibodies. Hence, determination of the Rh status in all obstetric patients and in all patients undergoing surgery or likely to be transfused is important. A complete premarital, prenatal, and pretransfusion examination should include this procedure. Potent *human* anti-Rh serum is to be used for such determinations as the various animal serums have not been entirely satisfactory.[6] It is of vital importance that every Rh-negative woman receive Rh compatible blood. This is essential not only to protect her from a transfusion reaction, but also to avoid stimulation of Rh antibodies which may cause, in the future, congenital hemolytic anemia and subsequent transfusion reactions. There is, as a rule, no harm in administering Rh-negative blood to an Rh-positive woman. Therefore, if the Rh status of a patient to be transfused is unknown, Rh-negative blood should be administered.

The obstetrician's responsibility does not end with mere determination of the patient's Rh type. If a pregnant woman is Rh negative, the blood of her husband and children, if any, should be tested also, and a careful history taken of any previous pregnancies and transfusions. When the husband is Rh positive, and there is a history of stillbirths or children with congenital hemolytic anemia, or of previous blood having been administered, either intravenously or intramuscularly, careful tests should be made for the presence of Rh antibodies. These should include the conglutination method of Wiener[7]; since the usual technique will not detect blocking antibodies. The tests are delicate but accurate, and should be repeated periodically during the pregnancy, especially after the seventh month. When these antibodies have been found, it is the obstetrician's duty to notify the pediatrician and to have Rh-negative blood available for both mother and child. Cases of congenital hemolytic disease should be transfused with Rh-negative blood as soon as anemia develops. If other Rh-negative blood is not available, a saline suspension of the maternal red cells which have been washed to remove the Rh antibodies may be used satisfactorily.

Recently, Polayes[8] and others[9, 10] have found that incompatibility between the A and B blood factors may also be the cause of congenital hemolytic anemia. A high titer of anti A or anti B agglutinins in a mother with a group A, B, or AB fetus may cause this condition. It follows, therefore, that stimulation of antibodies causing an increase in the titer of anti A or anti B agglutinins is to be avoided in females capable of childbearing, as a subsequent pregnancy may result in an infant with congenital hemolytic anemia. Such stimulation may be brought about by the administration of pooled plasma, the injection of incompatible whole blood, a practice once commonly employed in infants, and by the parenteral use of any solution containing group specific substances A and B.[11]

It is not sufficient that adequate supplies of whole blood of the various groups are on hand. Provision must be made for emergency transfusions. The admission to obstetric and gynecologic wards of women suffering from hemorrhage and shock due to placenta previa, abruptio placenta, ruptured ectopic pregnancy, and incomplete abortion, to mention a few, is a daily occurrence. Unexpected and alarming hemorrhage in the delivery room and on the wards is not uncommon. Proper treatment demands immediate replacement of blood. Even when the patient's blood group and Rh status is known, accurate cross-matching tests require time, and the resulting delay may be detrimental to the patient. While such tests are being made, "universal donor" Rh negative group O blood, with a low titer of iso-agglutinins, should be given at once and continued until properly matched blood is available.[12] The indiscriminate use of random group O blood as universal donor blood is condemned, as such blood may contain a high titer of iso-agglutinins and cause a severe hemolytic reaction. Group O blood in which the agglutinin titer has been reduced by the addition of group specific substances A and B is not recommended for use in women potentially capable of pregnancy, because these substances may cause increased iso-antibody formation as previously noted.[11]

During the emergency treatment of shock and hemorrhage, it is often impossible to insert a needle into the patient's collapsed veins. In such instances

transfusion by the intrasternal route or via the femoral vein is as feasible and efficacious as the usual technique. Both of these methods have been found to be satisfactory in the treatment of severe battlefield casualties. Another point to be remembered is that the proper management of hemorrhage requires adequate replacement of the blood lost. A pint of blood given to a woman who has lost 1,500 c.c. may have little effect beyond a false sense of security to the attending physician. The amount of blood transfused should at least equal the amount lost. The speed of transfusion may also be quite important in emergency cases. There is no reason in such instances why blood may not be given by several routes at the same time. The rate of the usual transfusion should be between fifty and sixty drops a minute, but for severe hemorrhage and shock, blood should be transfused as quickly as possible and under pressure if necessary.

Blood transfusions are not without danger. Severe and fatal reactions may occur following their use. However, serious complications are invariably due to improper or imperfect technique. Reactions following whole blood transfusions may be classified into three main groups: (1) pyrogenic or thermal, (2) hemolytic, and (3) allergic.

Pyrogenic or thermal reactions are characterized by chill and fever occurring during or shortly after the transfusion. They are caused by the presence of either foreign substances or toxic products of bacterial growth called pyrogens, as the result of improper preparation of the preserving solution or of the tubing and needles used during the collection and administration of the blood. This type of reaction can be entirely eliminated by strict adherence to a pyrogen-free technique.[2]

Hemolytic reactions are caused by the administration of either group or Rh incompatible blood, and may occasionally be due to rare iso-agglutinins such as anti Hr and anti M. They are usually described as consisting of chill, fever, pain in the lumbar region, hemoglobinuria, and, if severe, oliguria, anuria, and subsequent death. Recent experiments have demonstrated that the clinical symptoms of chill, fever, and lumbar pain are present in less than 50 per cent of severe hemolytic reactions.[12] Their absence, therefore, does not preclude such a complication. Hemoglobinuria and an increased bilirubinemia are constant findings in this type of reaction. The first post-transfusion specimen of urine should be examined routinely for hemoglobin. Careful attention to grouping and crossmatching tests prior to transfusion will prevent most, if not all, hemolytic reactions.

Allergic reactions are manifested as a rule by urticaria of varying degree and severity. Occasionally, asthmatic attacks may follow transfusions. True anaphylactic shock is very rare. At the present stage of knowledge, allergic reactions cannot be eliminated. However, the use of donors who have fasted for several hours prior to their blood donation and who do not have a history of severe allergy may reduce the incidence of such reactions.

In a well-organized and properly conducted transfusion service, the reaction rate will not exceed 2 per cent. These will be mainly of the allergic type, with a few pyrogenic in nature. Hemolytic reactions should not occur.

When a reaction of any severity occurs, the transfusion should be stopped immediately, and another bottle of compatible blood given with fresh transfusion

apparatus. The remaining portion of the blood causing the reaction should be sent to the laboratory together with 10 c.c. of the patient's freshly drawn blood and the first specimen of urine voided. Careful grouping and cross-matching tests should be performed again. The patient's blood is examined for increased bilirubin content, and the urine for hemoglobin and increased urobilinogen. The presence of hemoglobinuria or an increased bilirubinemia is definite evidence of a hemolytic reaction.

Pyrogenic reactions require no therapy other than symptomatic. Allergic reactions respond well to small doses of epinephrine. The treatment of hemolytic reactions consists in the transfusion of compatible blood and glucose and saline infusions. There is no evidence to support the theory that alkalinization of patients prior to transfusion will prevent the occurrence of reactions or lessen their severity.

When whole blood is available, the use of blood plasma in obstetrics and gynecology should be restricted to the treatment of shock without hemorrhage. Lacking whole blood, blood plasma is invaluable for the emergency treatment of hemorrhage and should be transfused until whole blood can be given. As previously mentioned, recent investigations have presented evidence that the administration of pooled plasma to females potentially capable of childbearing may cause congenital hemolytic anemia in subsequent pregnancies. This is predicated on the following facts. Pooled plasma is usually obtained from the bloods of all four blood groups, and hence will contain both A and B factors. These A and B factors are capable of stimulating the increased formation of iso-agglutinins, if administered to persons of blood group A, B, or O. A high titer of maternal iso-agglutinins can cause congenital hemolytic anemia in a fetus of a different blood group. For example, a group A fetus may have congenital hemolytic anemia caused by a high titer of anti A iso-agglutinins in its group O mother. Hence, the use of any substance which can increase the iso-agglutinin titer of women potentially capable of pregnancy is to be avoided. Therefore, the use of blood plasma in such women should be restricted to group compatible plasma. Group O plasma with a low titer of iso-agglutinins is also acceptable, since it does not contain the A or B factors.

It is granted that there is only a small possibility of such complications occurring following the use of pooled plasma. Certainly until more ample supplies of whole blood and plasma are available to permit the use of compatible plasma, no one should hesitate to administer pooled plasma when indicated.

Reactions following plasma transfusions are similar to those occurring after the administration of whole blood, although there is only a slight possibility of hemolytic reactions due to plasma. Plasma does not contain red cells, at least in significant quantities. Hence, there is no danger of a reaction caused by hemolysis of donor cells by recipient's serum. This is the major cause of hemolytic reactions. However, a plasma with a high titer of anti A or anti B iso-agglutinins can cause very serious hemolytic reactions, if given to an incompatible recipient.[12] This is the reason why plasma is pooled from all the blood groups. Properly pooled plasma, because of its low iso-agglutinin titer, will not cause a hemolytic reaction.

Human albumin, a product of the fractionation of whole blood, is of little interest to the obstetrician and the gynecologist. It may be used occasionally in pernicious vomiting of pregnancy, hypoproteinemia, nephrosis, and debilitated states. However, in all of these instances amino acid preparations are more effective when intravenous protein therapy is indicated.

The various preparations offered as substitutes for whole blood and human plasma, including bovine albumin, gelatin, sodium arabinate, pectin, and isinglass have not been found satisfactory, and some are actually harmful. An ample supply of whole blood and plasma will make their use unnecessary.

Red-cell suspensions are useful in the treatment of anemias. These suspensions are usually obtained as a by-product of the processing of whole blood for plasma. Since the Army and Navy have recently released a large supply of blood plasma to civilian hospitals, less blood will need to be converted into plasma. This will reduce the amount of red-cell suspensions available. It will, therefore, be more practical to use whole blood for the therapy of anemias.

Summary

Blood transfusions are an essential form of obstetric and gynecologic therapy. In view of the recent advances in the knowledge of this subject, obstetricians and gynecologists have a definite threefold responsibility: (1) To have an ample supply of whole blood and plasma available. This can be assured by the establishment of a community blood bank such as suggested by the Red Cross. (2) To demand that the collection, preservation, and administration of whole blood and plasma conform to the best technical standards. The adoption of the closed system vacuum technique and the use of the ACD preserving solution will meet such criteria. (3) To insure that blood or plasma administered to their patients must be beneficial without reaction, and to avoid antibody stimulation which may subsequently cause difficulties in later pregnancies or transfusions. This can be accomplished under a pyrogen-free technique by the use of group and Rh compatible blood for routine transfusions, of Rh-negative group O blood with a low titer of iso-agglutinins for emergency transfusions, and of group compatible or group O plasma with a low iso-agglutinin titer when plasma is indicated.

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THE ANTEPARTUM PREDICTION OF HEMOLYTIC DISEASE OF THE NEWBORN*

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DESPITE the intensive researches on the relationship of erythroblastosis fetalis to the Rh factor, the obstetrician is handicapped because he is unable to forecast the outcome of pregnancy in Rh-negative women. Not only is he in doubt about the presence or absence of erythroblastosis fetalis in utero, but he is also unable to predict its gravity when there are reasonable clinical indications that it may exist. As will be shown in a separate communication,[1] the mere existence of either anti-Rh agglutinins or "blocking antibodies" in the maternal serum antepartum—whether these substances increase, decrease, or disappear—is not necessarily correlated with the existence of hemolytic disease of the newborn, nor with its severity.

The present study is confined to an analysis of an apparent correlation between the duration of exposure of the fetus to maternal Rh antibodies and the prognosis for the newborn child. Inspection of these data discloses a partial answer to the obstetrician's dilemma. The material subjected to analysis was selected from a sample of over 4,000 pregnant women seen in the obstetric clinic of the University of California Hospital and in the private practices of six obstetricians, who submitted regular antepartum blood samples for study. The blood serum from each patient was tested for agglutinating antibodies against two Rh negative group O, and two Rh positive group O red blood corpuscle suspensions. The presence of blocking antibodies was determined by the method of Wiener.[2]

In the majority of instances, the first blood sample was not obtained until the third trimester of pregnancy. Thus, when antibodies were found at this time, it was impossible to know when they had first appeared. The appearance time, however, could be dated in 26 cases, and it was immediately apparent that no cases of erythroblastosis occurred when the antepartum duration of antibodies was ten weeks or less. In all cases, the "appearance time" was estimated to be midway between the time of the last negative sample and the time of the first positive sample. In the remaining material, it was therefore logical to exclude all cases in which the first blood sample had been obtained less than ten weeks before delivery, but to include those in which the first positive sample was obtained "more than eleven weeks" or "more than sixteen weeks," et cetera, before parturition.

After such exclusion, 49 cases remained for analysis. By inspection, it was noted that in 19, only "traces" of either agglutinating or blocking antibodies had been found, or there had been an isolated finding of a small ("one plus"

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or "partial") amount of either type of antibody which was unconfirmed by subsequent and repeated tests. Only one case of possible erythroblastosis fetalis occurred in this group, that of a baby who had a slight increase in the number of nucleated red blood cells at birth, and who suffered from a mild anemia which did not require transfusions.

In the remaining 30 cases, appreciable amounts of antibodies were found, or small amounts were present on repeated occasions. In 22 of these cases, the antibodies appeared more than ten weeks before delivery, and all 16 cases of erythroblastosis fetalis were found in this group. The remaining six women were delivered of normal infants, four of whom proved to be Rh-negative children of mothers who had been previously sensitized, and presumably this pregnancy had elicited a nonspecific anamnestic recall of Rh antibodies. Unfortunately, there was no way of differentiating antepartum the mothers of these four cases from those who were carrying Rh-positive infants. The remaining two exceptions cannot be explained.

TABLE I. THE RELATIONSHIP OF THE APPEARANCE TIME OF RH ANTIBODIES BEFORE DELIVERY TO THE OCCURRENCE AND SEVERITY OF HEMOLYTIC DISEASE OF THE NEWBORN

ANTIBODY APPEARANCE (NO. WEEKS ANTEPARTUM)	CASES WITH "TRACES" OR AN ISOLATED SMALL AMOUNT OF ANTI-RH OR BLOCKING SUBSTANCE	CASES WITH LARGER AMOUNTS OF ANTIBODIES, OR WITH SMALL AMOUNTS WHICH WERE REPEATEDLY CONFIRMED*	
		Rh+ infants	Rh– infants
1 to 9	8—All normal	7—All normal	1—normal
10 to 14	3—All normal	8 { 1 normal; 3 "subclinical"; 4 icterus gravis (3 deaths)	2—Both normal
15 to 36	8 { 7 normal; 1 questionable "subclinical"	10 { 1 normal; 1 hemolytic anemia; 1 icterus gravis; 7 hydrops fetalis (7 deaths)	2—Both normal

*Cases with positive antibodies on first samples obtained less than ten weeks before delivery were excluded (see text).

The results of classifying these cases as described are summarized in Table I. The influence of the appearance time of antibodies upon the prognosis is further emphasized when the ten- to fourteen-week period is studied separately from the fifteen- to thirty-six-week period. Hemolytic disease of the newborn varies in its severity from the mildest subclinical variety through the simple, though often severe, anemia to the "icterus gravis" form, in which there is widespread pigment deposition at birth, and finally to the universally fatal "hydrops fetalis" with its widespread visceral damage and generalized edema. All of the mild (subclinical) cases occurred in the ten- to fourteen-week group. Of the eight Rh-positive babies in this group, seven had hemolytic disease, and of these, three died of icterus gravis. On the other hand, *all seven cases of fatal hydrops fetalis were found in the 10 Rh positive infants* of the group in which maternal antibodies had appeared at least *fifteen weeks* or more before the delivery.

If such figures as these are confirmed by subsequent study of a larger series, it becomes obvious that the induction of premature labor is unnecessary when

Rh antibodies first appear less than ten weeks from term, and probably useless when they appear more than fifteen weeks from the time selected for induction of labor. The termination of pregnancy by conservative means and prompt transfusion* of the anemic child at birth should result in a higher survival of infants only in that small group of mothers wherein antibodies appear for the first time ten to sixteen weeks before the estimated date of confinement. Beyond that period, any attempt to reduce the exposure to ten weeks or less would probably result in the loss of the child from prematurity, or from a combination of prematurity and erythroblastosis. Eleven of the cases included in this study were primigravid women, and in all but one the antibodies appeared late in pregnancy, which probably explains why first babies characteristically, but not invariably, escape the disease.

These findings may be summarized and translated into tentative suggestions for the management of obstetric patients as follows:

Ideally, all pregnant women should be typed routinely, regardless of parity, and in those Rh-negative patients having Rh-positive husbands, the first sample of blood for antibody determination should be obtained not later than the twenty-fourth week of pregnancy. If this be strongly positive for either agglutinating or blocking antibodies, an Rh-positive fetus will probably be too seriously affected by hemolytic disease to warrant any interference before term, while an Rh-negative fetus will escape the disease. As yet, there is no way to distinguish these possibilities except to prove that the father is homozygous for the Rh factor. If the antibodies are present only in "traces," or if a small amount is found on a single determination and is unconfirmed by subsequent tests, the fetus is probably unaffected, and again it would be unwise to interfere.

If the initial sample is free of antibodies, but a significant amount appears later, a period of eight to ten weeks may be allowed to pass before hemolytic disease becomes a probability. After this time, induction of labor might be warranted providing the expected date of confinement is within the ensuing six weeks.

That a relationship exists between the duration of exposure to maternal antibodies and the fetal prognosis seems apparent. Further study may alter the critical time periods established by the data of this preliminary analysis.

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*It is recommended that an immediate slow transfusion of 50 to 75 c.c. of Rh-negative group O blood be given into the umbilical vein.

BACTERIOLOGY OF THE ORONASAL CAVITY OF THE NEWBORN

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A KNOWLEDGE of the organisms that are found in the oronasal cavity of the newborn under routine conditions of labor and delivery in a hospital is of great practical importance to the clinician. It furnishes information relative to the organisms normally present under these circumstances, so that their relationship as secondary invaders to a primary infection can be better understood. It also sheds light on the types of organisms which frequently contaminate the newborn during labor and delivery and their probable source.

Some information on this problem is afforded by the results obtained by other investigators on studies of the bacterial flora of the human vagina, skin, and rectum. Of major importance is the question of whether puerperal infections are intrinsic or extrinsic in origin, and likewise whether infections of the newborn child are obtained from the mother or are extrinsic in origin.

Lancefield and Hare[1] examined by the precipitin test a large number of hemolytic streptococci which had been obtained from women suffering from puerperal infections and from women with afebrile puerperia. Forty-five out of 46 strains isolated from puerperal fever cases fell into Lancefield's Group A, while only one out of 65 strains isolated during afebrile puerperia was *Streptococcus pyogenes.* Of 13 strains isolated from vaginas before labor, none was *Str. pyogenes.* Colebrook, Maxted, and Johns[2] failed to detect *Str. pyogenes* on the perineal or perianal skin of 160 women during pregnancy, while Hare and Maxted[3] failed to isolate *Str. pyogenes* from the feces of 100 normal women during the first stage of labor.

In 1938, Weinstein[4] published a critical report on the bacterial flora of the human vagina under varying conditions of disease and of pregnancy. Of 375 patients examined, staphylococci were isolated 254 times. Eleven were hemolytic *Staphylococcus aureus* isolated from pregnant women who subsequently suffered no complications at parturition or in the puerperium. Hemolytic streptococci were isolated 29 times, but no effort was made to type them. *Escherichia coli* was found to be present in only 27 of the cases studied, which refutes the common belief that it is a frequent inhabitant of the vaginal tract. No appreciable difference could be detected in the flora obtained from pregnant, nonpregnant, or in healthy and diseased genital tracts.

Carter and his associates[5] cultured the yeastlike fungi from the vagina and vulvas of 200 pregnant women and found an incidence of 86 positives for these fungi, of which 20 were classified as *Candida albicans.*

Materials and Methods

Immediately following delivery, before the oral and nasal cavities of the infants had been aspirated of mucus, sterile cotton applicators were directed into the posterior oronasal pharynx and nasal orifices, using careful aseptic

technique. Two applicators were used on each infant, the first of which was placed immediately in sodium azide broth, while the second applicator was used to streak MacConkey's agar and Sabouraud's glucose agar plates.

In the first series of 100 unselected newborn infants, a specific attempt was made by the use of selective media to isolate staphylococci, coliform bacilli, and moniliae. The staphylococci were isolated according to the method of Pike.[6] Sodium azide blood enrichment broth was inoculated by placing the oronasal swab in the broth and incubating twenty-four hours at 37° C. Brain and heart infusion blood agar was streaked from this broth, incubated overnight at 37° C., and any hemolytic staphylococci picked and tested for coagulase activity. Coliform organisms were determined by direct streaking of MacConkey's medium with the oronasal swab and incubating at 37° C. for twenty-four hours. Yeast-like fungi were found by direct streaking of Sabouraud's glucose agar with the oronasal swab and incubating at 37° C. for a period of seven days. *Candida albicans* strains were identified by the formation of chlamydospores on corn meal agar together with their fermentation reactions in glucose, maltose, sucrose, and lactose broths. All yeasts not producing mycelia in corn meal agar were tested for ascospore formation on potato glucose agar.

A second series of 50 unselected newborn infants was studied with special reference to streptococci and pneumococci. Approximately 0.5 ml. of aspirated material from the newborn infant's oral and nasal cavities was placed in a sterile test tube. At the same time, an oronasal swab was placed in sodium azide crystal-violet blood enrichment broth devised by Pike[6] for streptococci and incubated overnight at 37° C. Brain heart infusion blood agar plates were streaked from this enrichment broth, incubated twenty-four hours at 37° C., and examined for alpha and beta hemolytic streptococci.

The aspirated material in each test tube was injected intraperitoneally into a mouse for the detection of pneumococci. All mice living at the end of twenty-four hours were sacrificed, and a swab of the abdominal cavity streaked on brain heart infusion blood agar. After incubation at 37° C. for twenty-four hours, colonies showing alpha hemolysis were examined for pneumococci.

TABLE I. BACTERIAL ORGANISMS FOUND IN THE ORONASAL CAVITIES OF NEWBORNS WITH DELIVERIES GROUPED ACCORDING TO LENGTH OF TIME MEMBRANES WERE RUPTURED BEFORE BIRTH

DELIVERIES*				
NUMBER	PER CENT	STAPHYLOCOCCI	COLIFORM	MONILIAE
		Membranes Ruptured 1 to 12 Hours		
38	42.0	−	−	−
30	33.0	+	−	−
10	11.0	−	+	−
4	4.4	+	+	−
4	4.4	−	−	+
2	2.2	−	+	+
2	2.2	+	−	+
1	1.0	+	+	+
		Membranes Ruptured 12 to 24 Hours		
1	16.6	−	−	−
3	50.0	+	−	−
1	16.6	−	+	−
1	16.6	+	+	−
		Membranes Ruptured 24 to 72 Hours		
1	33.3	+	+	−
1	33.3	+	−	+
1	33.3	+	+	+

*Afebrile patients.

Findings and Results

Thirty-nine of the first series of 100 cultures from newborn infants were negative for staphylococci, coliform bacilli, and moniliae, Table I. Forty-four strains of hemolytic staphylococci were isolated, two of which were coagulase positive. Twenty-one plates positive for coliform organisms were found, with 11 of them showing the cultural characteristics for *E. coli*. Of the 11 yeast strains isolated, only two were *Candida albicans*.

All three deliveries in which the membranes had ruptured twenty-four to seventy-two hours prior to delivery showed positive cultures in the infants for staphylococci, coliform bacilli, or streptococci (Table I). There were 83 per cent positive cultures for six infants in which the mother's membranes had been ruptured twelve to twenty-four hours prior to delivery, while only 58 per cent of 91 infants had positive cultures when the mother's membranes had been ruptured one to twelve hours before delivery.

There were two neonatal deaths which at autopsy yielded reports of atelectasis and subdural hemorrhage, and cerebral hemorrhage, respectively.

There were 22 spontaneous, 55 elective low forceps, 19 low forceps, two midforceps, and two elective cesarean section deliveries.

TABLE II. BACTERIAL ORGANISMS FOUND IN THE ORONASAL CAVITIES OF NEWBORNS WITH DELIVERIES GROUPED ACCORDING TO TYPE OF DELIVERY

DELIVERIES*				
NUMBER	PER CENT	STAPHYLOCOCCI	COLIFORM	MONILIAE
		Spontaneous Deliveries		
8	36.4	-	-	-
6	27.3	+	-	-
3	13.6	-	+	-
2	9.1	+	+	-
2	9.1	-	-	+
1	4.5	-	+	+
		Low Forceps Deliveries		
29	39.2	-	-	-
25	33.8	+	-	-
8	10.8	-	+	-
4	5.4	+	+	-
2	2.7	-	-	+
1	1.4	-	+	+
3	4.0	+	-	+
2	2.7	+	+	+
		Midforceps Deliveries		
2	100.0	+	-	-
		Cesarean Section Deliveries		
2	100.0	-	-	-

*Afebrile patients.

According to Table II, 64 per cent of the infants' oronasal cavities yielded positive cultures for staphylococci, coliform, or moniliae when delivery occurred spontaneously, as compared to 61 per cent positive cultures when delivery was by low forceps. The two midforceps cases gave positive cultures for staphylococci, while two cesarean sections were negative for the three organisms studied.

In the second series of 50 cases, Table III, only streptococci and pneumococci were investigated. Pneumococci were not found by the methods used. However, six cases yielded alpha streptococci, and from four other cases beta streptococci were isolated. The beta strains were tested by Lancefield's precipitin reaction and found to be negative with groups A, B, and C antisera. All strains of streptococci including both alpha and beta were able to grow at 45°

TABLE III. BACTERIAL ORGANISMS FOUND IN THE ORONASAL CAVITIES OF NEWBORNS WITH DELIVERIES GROUPED ACCORDING TO LENGTH OF TIME MEMBRANES WERE RUPTURED BEFORE BIRTH, SECOND SERIES

DELIVERIES*			
NUMBER	PER CENT	STREPTOCOCCI	PNEUMOCOCCI
		Membranes Ruptured 1 to 12 Hours	
35	85.0	–	–
5	12.5	alpha +	–
1	2.5	beta +	–
		Membranes Ruptured 12 to 48 Hours	
5	55.5	–	–
1	11.0	alpha +	–
3	33.5	beta +	–

*Afebrile deliveries.

C. and were not killed by heating at 60° C. for thirty minutes. From these results it was concluded that these organisms belonged to the enterococcus group of streptococci, *Streptococcus fecalis.* (Group D antiserum unavailable.)

According to Table III, a predominance of beta streptococci (33.5 per cent) were present when the membranes had been ruptured twelve to forty-eight hours, as compared to 2.5 per cent for the shorter period of one to twelve hours. There were also a predominance of beta streptococci (11 per cent) present, Table IV, when delivery was by low forceps, as compared to no beta streptococci in the spontaneous deliveries. In this series, there were 13 spontaneous, four low forceps, and 33 elective low forceps deliveries. There were no mid-forceps, cesarean sections, or febrile patients.

Special mention should be made here of three patients in the first 100 series who were febrile intrapartum, Table V. Two of the infants had positive staphylococci cultures, while the other had a positive coliform culture.

TABLE IV. BACTERIAL ORGANISMS FOUND IN THE ORONASAL CAVITIES OF NEWBORNS WITH DELIVERIES GROUPED ACCORDING TO TYPE OF DELIVERY, SECOND SERIES

DELIVERIES*			
NUMBER	PER CENT	STREPTOCOCCI	PNEUMOCOCCI
		Spontaneous Deliveries	
11	85.0	–	–
2	15.0	alpha +	–
0	0	beta +	–
		Low Forceps Deliveries	
29	78.0	–	–
4	11.0	alpha +	–
4	11.0	beta +	–

*Afebrile deliveries.

TABLE V. BACTERIAL ORGANISMS FOUND IN THE ORONASAL CAVITIES OF NEWBORNS WHOSE MOTHERS HAD INTRAPARTUM FEVERS

Febrile Patients			
NO. OF DELIVERIES	STAPHYLOCOCCI	COLIFORM	MONILIAE
1	–	+	–
2	+	–	–

Discussion

These 150 oronasal cultures were obtained from consecutive deliveries in a private institution staffed by both the general practitioner and specialist. No effort was made to change the labor or delivery care of these patients by the

attending physicians for this series, thus the results comprise a representative cross section of obstetric practice under the labor and delivery circumstances of this institution.

Only one case had been given chemotherapy prior to delivery. This patient was a severe pre-eclamptic whose membranes had been ruptured twenty hours prior to delivery. Even though she was afebrile, 1 Gm. of sulfadiazine was orally administered prophylactically. Bacteriologic cultures of this newborn's oronasal cavity yielded coagulase positive staphylococci and coliform bacilli.

In Table I, the bacteriologic data from the first series of 100 deliveries was arranged according to the length of time the membranes had been ruptured. There was a marked increase in the percentage of positive cultures obtained when the membranes had been ruptured a long time as compared to the shorter periods. This percentage ranged from 42 per cent for the shorter interval of one to twelve hours to 100 per cent in the longer period of twenty-four to seventy-two hours. This observation should be of significance to the obstetrician.

In Table II, the above data from the first 100 deliveries was rearranged to correlate bacteriologic results with types of deliveries. A study of this table reveals no significant differences between the use of low forceps and the occurrence of spontaneous deliveries. Midforceps were used in only two cases, which is too small a number from which to draw any conclusion.

The results obtained in the search for pneumococci and streptococci suggest that streptococci causing puerperal fever are probably extrinsic in origin and also that pneumococci capable of infecting the infant are not normal inhabitants of the vagina.

There was a larger percentage of beta streptococci present when the membranes had been ruptured a long time or whenever forceps were used. However, the small number of streptococci found does not give these results significance.

Weinstein[4] found the vaginal flora to contain staphylococci in 67 per cent and beta-hemolytic streptococci in 8 per cent of the 375 women studied, while the results of this study showed 44 per cent positive for staphylococci (first series) and 8 per cent for beta-hemolytic streptococci (second series).

Moniliae of the *Candida albicans* type are not infrequently found in the vaginas of pregnant women and they may or may not have clinical importance. In this series from 100 oronasal cultures, eleven yeastlike fungi were isolated of which two were classified as *Candida albicans*. Thus, two infants had *Candida albicans* present in their oronasal cavities, but which showed no clinical signs of thrush.

E. coli were present in a larger percentage of cases than would have been expected on the basis of other work. These bacteria were found in 11 per cent of this series, while Weinstein[4] recorded only 6 per cent. The high incidence of *E. coli* organisms was undoubtedly due to fecal contamination during parturition.

It is also of cogent interest to point out here that according to our results it is possible to have deliveries which show a minimum contamination of the newborn infant's oronasal cavity.

Conclusions

1. The oronasal cavity of the newborn has been found to contain staphylococci, the enterococcus group of streptococci (*Str. fecalis*) and moniliae in approximately the same ratio as other investigators have found them to be present in the vaginal tract of the pregnant woman. On the other hand, a much higher percentage of *E. coli* organisms were present in the infant's oronasal cavity than previously reported for the pregnant vagina, which is presumed to represent contamination from the rectum in labor or during delivery.

2. A definite correlation was observed between the length of time the membranes had been ruptured and the frequency with which organisms were found in the oronasal cavity of the child. A larger percentage of infants were contaminated during longer than during shorter labors.

3. Pneumococci were not found in these cases, nor were streptococci of the puerperal fever type found. Only two of the 44 strains of staphylococci were coagulase positive. Eleven yeastlike fungi were isolated of which two gave the true characteristics of *Candida albicans.*

The authors wish to express their appreciation to the medical staff of St. Joseph's Maternity for its wholehearted cooperation in making all their patients available for inclusion in this study, and also to the nursing and record room staffs for their helpful assistance.

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MENORRHEAL PROBLEMS IN COLLEGE WOMEN*

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NINETEEN thousand, two hundred and eighty-three women entered the University of Minnesota from 1935 to 1945. Of these, 5,210 women consulted the gynecologic department of the Student Health Service. Most of these were between the ages of 18 and 25 years. The three common symptoms which brought the students to this department were: pain, vaginal discharge, and irregular bleeding. One thousand, six hundred and sixty-seven women came in because of irregular bleeding, an incidence of 32 per cent. The term "menorrhea" might be used to include all of the factors associated with periodic bleeding from the uterus. The changes of the endometrium are controlled by a complex endocrine mechanism. Obviously, uterine bleeding may occur under many conditions.

Before a scientific treatment of menorrheal bleeding is possible, one must understand the physiology of menstruation. The physiologic purpose of the uterus is to house and nourish the fertilized ovum to maturity. If menstruation is to be considered a normal phenomenon, then it must be due to the change in a normal structure. It may be more satisfactory to limit the term menstruation to bleeding which occurs from an endometrium which has undergone the cycle of changes necessary for nidation, and the presence of a fertilizable ovum. All of the endocrine glands probably influence the menstrual cycle. It is dependent upon the hormones of the anterior pituitary gland, the response of the ovary, and the response of the uterus to both the pituitary and ovarian stimulation. The appearance of the ovaries and uterus may vary during successive periods in the same woman or at the same stage in different individuals.

The menstrual cycle may be divided into three phases: (1) the proliferative, estrogen, or preovulatory phase; (2) the secretory, progestin, or postovulatory phase; and (3) the menstrual or dismantling phase. Some authors further divide the phases into repair phase, resting phase, and early and late secretory phases. The menstrual phase is attended by bleeding from the spiral arterioles with the exfoliation of the compacta and the spongiosa layers of the endometrium, leaving only the basal layer intact.

The literature on menorrheal irregularities is confusing because of the discrepancy of terms used. Uterine bleeding may be divided into two main categories: disturbances of menstruation, and nonmenstrual bleeding. Uterine bleeding will continue until healing by epithelization occurs. The amount of bleeding depends upon the size of the vessels involved and their resistance to closure by natural or mechanical means. A modified Schroeder classification has been used as a basis to sort out the various types of bleeding. As more information is available from hormone studies and endometrial curettings, the subdivisions of the following classification will become apparent.

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A. *Disturbances of Menstruation*

I. Disturbances in the regularity of the cycle
- a. Shortened cycle (polymenorrhea)
  - 1. Premature interruption of the cycle
- b. Lengthened cycle (oligomenorrhea)
  - 1. Persistent corpus luteum
  - 2. Hyperplasia of the endometrium
  - 3. Inhibited cycle followed by a normal cycle
- c. Amenorrhea
  - 1. Physiologic
  - 2. Primary amenorrhea
  - 3. Secondary amenorrhea
- d. Acyclic bleeding (metrorrhagia)

II. Disturbances in the amount of menstrual flow
- a. Profuse flow (hypermenorrhea)
  - 1. Hypoplastic uterus
  - 2. Hypothyroidism
  - 3. Tumors (polyps, submucous myomas)
  - 4. Pelvic congestion
  - 5. Endometrial hyperplasia
- b. Scanty flow (hypomenorrhea)
  - 1. Hypogonadism
  - 2. Hyperthyroidism

III. Disturbances in the duration of menstrual flow
- a. Lengthened bleeding period (menorrhagia)
  - 1. Irregular shedding and irregular ripening
  - 2. Endometrial hyperplasia
  - 3. Inflammatory
  - 4. Tumors (benign or malignant)
- b. Shortened bleeding period.
  - 1. Hypogonadism

B. *Nonmenstrual Bleeding*

I. *Disturbances under ovarian control*
- a. Cystic glandular hyperplasia
  - 1. Granulosa-cell tumors
- b. Ovulation bleeding
- c. Anovulatory bleeding
- d. Following hormone treatment

II. Disturbances not under ovarian control
1. Uterine, acyclic bleeding (metrorrhagia)
   - a. Tumors (polyps, myomas)
   - b. Incomplete abortion
   - c. Infection
   - d. Malignancy
2. Adnexal
   - a. Tumors
   - b. Pelvic inflammatory disease
3. Blood dyscrasias
   - a. Purpura hemorrhagica
   - b. Leucemia
   - c. Aplastic anemia
4. Constitutional diseases
   - a. Congenital syphilis
   - b. Tuberculosis

c. Cardiac decompensation
d. Graves' disease
e. Nervous disorders (shocks, fright)

A detailed history by systems and a general physical examination was done on each student before she consulted me. The examination included a general physical examination, blood serology, Mantoux test, hemoglobin, and urinalysis. A gynecologic history and a careful one-finger bimanual pelvic and/or a rectal examination was made on every woman who had gynecologic complaints. When indicated, other studies were done, including basal metabolism rate; serum cholesterol; prothrombin, bleeding and clotting time, and platelet count; erythrocyte and leucocyte count with differential; sedimentation rate; and x-ray of the sella turcica. Vaginal smears were taken with a pipette and stained according to the method of Papanicalaou, but in this age group they were not very helpful. Endometrial biopsies were not done except after a curettage had previously been performed. Parental permission for any surgical procedure is required for our college students.

Abnormal uterine bleeding may be divided into two groups: (1) disturbances of the endocrine glands, and (2) bleeding associated with constitutional diseases.

I. *Disturbances of the Endocrine Glands.*—

A. *Cystic glandular hyperplasia* is probably due to a dysfunction of the anterior pituitary gland with secondary ovarian failure. In hormone assays done on a patient with this condition, the estrin output in the urine was maintained at a high level. A diagnostic curettage is done when possible if hyperplasia is suspected. The typical "Swiss cheese" picture is frequently lacking. However, usually the curettings are abundant, and the glands are irregular in size and shape, and nonsecretory, indicating an exaggeration of the proliferative phase. One hundred and ten cases of hypermenorrhea and/or menorrhagia were seen. Of these, 62 improved under thyroid medication, the dose being pushed to three times the daily dose during the flow. Because of profuse flow, a diagnostic curettage was done on 24 patients with hypermenorrhea and/or menorrhagia. Ten, or 41 per cent, had less bleeding in cycles following curettage. A hyperplastic endometrium was found in 19 patients. The remainder of the endometria showed proliferative phase, secretory phase, or polypoid type. In the bleeding phase, bed rest, elevating the foot of the bed, ergot, vitamin K, and blood transfusion was given as indicated, sometimes with large doses of estrogens or anterior pituitary-like substances. After the bleeding phase, equine gonadotrophin was given as follows: intramuscular injection of 10 Cartland-Nelson units of gonadogen, then 20 Cartland-Nelson units on alternate days for a total of 90 units, and this was followed by 1,000 units of chorionic gonadotrophin on alternate days for five doses. One series of injections took care of six, or 43 per cent, more of these patients. A second series was started on the seventh to ninth day of bleeding if it was prolonged. It is important to watch for serum reactions and, therefore, the intravenous injection was given in only one case. A high vitamin diet was prescribed and strenuous exercise advised,

as well as sufficient rest and relaxation. Ferrous sulfate was given when the hemoglobin was below 12 Gm.; and some received Fowler's solution. The hormone assays done under the direction of Dr. Leo Samuels and the Department of Physiology after the administration of gonadotrophins showed an increase in the output of estrin in the urine but did not affect the pregnanediol levels in our series. It must be kept in mind that gonadotropic hormones might produce polycystic ovaries. The use of x-ray or radium has never been necessary to control the bleeding in any of these cases, nor has a hysterectomy been performed in any of these young women.

B. *Irregular shedding* probably represents the corpus luteum phase. The normal tempo of the flow is maintained, but the regeneration of the endometrium is prolonged. The amount of flow is variable. A diagnostic curettage between the eight and tenth days of bleeding usually reveals the transition between the functioning phases, indicating a delay in healing. The peripheral glands are collapsed into peculiar shapes. The epithelium is in the secretory phase in part of the slide and proliferative in part. Hormone assays in irregular shedding indicate the excretion of pregnanediol continuing during the bleeding phase. Curettage alone cures about 50 per cent of these cases. Many must clear up spontaneously, because years ago I prescribed "sistomensin," moccasin snake venom, or calcium, during the bleeding phase with good results in 60 per cent of the cases. Thyroid and iodine medication also benefits this condition. Giving 1 mg. of diethylstilbestrol daily after the fifth day of bleeding and continuing for three weeks, together with 10 mg. daily of anhydro-hydroxy progesterone (pranone or pregneninolone) during the third week, has been followed by cures.

C. *Anovulatory bleeding* represents a premature interruption of the menstrual cycle. Many histories indicate painless menorrhea the first year or two after the beginning of catamenia. Painless uterine bleeding after the administration of estrogen in the first half of the cycle are frequent, and the flow is usually not quite normal and may be early. Are these not anovulatory cycles? No treatment is indicated unless there is a sterility problem.

It may be impossible to determine whether or not ovulation has occurred. In two cases of sterility only one peak of estrin was found in hormone assays of the urine. However, there is no quantitative method to determine ovulation. When the endometrium is secretory, we assume there is a normal functioning corpus luteum. Even with serial sections of both ovaries, very few can diagnose histologically an active corpus luteum.

D. *Oligomenorrhea* or infrequent cycles is a common finding in college women. Hormone assays in two cases of oligomenorrhea revealed an increase of ketosteroids in the androgen fraction of the urine. A persistent corpus luteum may cause a decidua-like reaction of the stratum compactum of the endometrium with a delayed menstruation. Many women with a delayed period start to flow following a pelvic examination. This may be a psychic effect, or it may also be due to the fact that the examiner may have ruptured the persistent corpus luteum. To reassure the patient that she requires no therapy usually suffices.

CASE 1.—A 21-year-old student presented herself in January, 1944, because she had not become pregnant after having been married for one year. Onset of catamenia occurred at 11 years of age. Periods were regular until 1940, then they occurred every twenty to twenty-three days with one day of scanty flow. During the past year the periods had become more infrequent, skipping up to four months. General examination was negative, except that she was slightly underweight. Her basal metabolic rate was minus 23 per cent to minus 8 per cent. The patient tolerated one grain of thyroid daily. Pelvic examination was negative, except the uterus was about two-thirds normal size. The patient had a moderate flow following stilbestrol and pranone, and then was given gonadotrophin, the one-two method, with no period following. The medication was discontinued, except for thyroid for a period of one year, during which time the patient had a scanty flow for one day every month or two. In November, 1944, the patient passed a uterine endometrial cast which had decidua-like cells. Dr. Robert Meyer said it was not due to pregnancy, but probably to a persistent corpus luteum. The patient became anxious for a pregnancy, because her husband was to be inducted into the Army. Fertility studies were made, and the x-ray of the tubes revealed patency. A Huehner test was also normal. A diagnostic curettage on the first day of bleeding revealed follicular phase of the endometrium in January, 1945. An endometrial biopsy in March on the first day of bleeding was nonsecretory. The patient skipped two periods and again passed a cast of the uterus May 12, 1945, similar to the previous cast. She had a two-day period in June, 1945, and delivered a full-term baby boy in March, 1946. The conclusion was that the patient ovulated in June without medication.

E. *Amenorrhea* in college women is usually secondary and due to change of environment. It is interesting to note a case of twin girls who had regular menstrual periods until they entered college. They both stopped menstruating, and one reported to me. I suggested her returning after the Christmas vacation, if she did not have a period; both of them had normal cycles while at home, but again the periods ceased when they returned to school.

Continued amenorrhea is the cause of much concern to the student and her parents. Substitution therapy is not a cure, but bleeding may be produced with diethylstilbestrol priming and combined with oral progesterone. Whether bleeding is produced from a proliferative or secretory endometrium has the same psychic effect upon the patient. Withdrawal of ovarian hormones initiates the usual menstrual behavior of the coiled arteries. Progesterone given during the first half of the cycle produced bleeding within seventy-two hours after withdrawal. Hormone shots are expensive and annoying to the patient. Producing a menorrheal flow by oral medication helps to reassure the student. Following the oral administration of stilbestrol and pranone, bleeding occurs within forty-eight hours of progesterone cessation. I usually prescribe it after six months of amenorrhea. Many of the students menstruate when they are home on vacation and require no therapy. Estrogens in large doses or over a long period of time may inhibit the pituitary and reduce the ovarian function.

In the past ten years, I have examined eight cases of primary amenorrhea. Three of these had normal secondary sex characteristics with no evidence of uterus or vagina. No treatment was given except to inform the student of her condition in two cases. In the third, the mother refused this information being given to her daughter, but gave her consent for an examination of the patient

under anesthesia. The remaining five cases had hypoplastic uteri, with hypogonadism and normal basal metabolic rates. Four of them had periodic bleeding following the administration of estrogens, 10,000 units every other day for three weeks and 5 to 10 units of progesterone intramuscularly given concomitantly with the estrogens the third week. No treatment was given the fourth week. This regime was repeated for three successive months unless uterine bleeding occurred. The one-two method of gonadotropic hormone injections was then given. The uteri of all of these women increased in size during the treatment, and the patients developed a feeling of well-being. One woman was overweight and was given thyroid also. The menorrheal period did not continue to be regular in any of these women without some stimulation six to twelve months later. However, usually stilbestrol and pranone were sufficient to bring on the bleeding once it was established. One of these students has married and has had one pregnancy. Since her pregnancy she again has an amenorrhea which has now persisted for six months, although she is not nursing her baby. One patient has never menstruated and has been advised against further endocrine therapy for the time being. She was given both types of treatment and also thyroid, the latter over a period of one year.

Secondary amenorrhea may be an early sign of dementia precox. It may also be due to constitutional causes. Physiologic amenorrhea is cared for by the patient's private physician, but a number of women come in for a diagnosis of pregnancy.

II. *Bleeding Associated With Constitutional Disorders.*—

The underlying cause obviously is treated when examination reveals the bleeding to be due to constitutional disorders. The university students are on the whole in excellent health, and chronic ailments are but rarely encountered. Bleeding due to the following conditions has not been evident in this group.

a. Granulosa-cell tumor of the ovary.

b. Blood dyscrasia (purpura hemorrhagica, aplastic anemia, and acute lymphatic leucemia).

c. Congenital or acquired syphilis.

d. Tuberculosis.

e. Graves' disease.

f. Cardiac decompensation.

g. Teratoma and sarcoma (four women had laparotomies and dermoid cysts of the ovaries were removed). Very few gynecologic laparotomies have been done on college students in the past five years because of the good economic conditions. The surgery is done by the student's private physician during the summer vacation.

h. Polyps of the cervix are very uncommon in this group.

i. Endocervicitis and cervicitis are treated by electrocautery, and usually one treatment suffices.

j. Pelvic inflammatory disease is uncommon. With sulfonamides and penicillin, the few acute Neisserian infections seen have been readily cured.

k. Malpositions of the uterus. Most of the retroversions of the uterus are apparently congenital in type and have no apparent relation to irregular bleeding.

1. Nervous disorders, shocks, and frights. (A fairly large number of hypermenorrhea and menorrhagia were seen each year attributed to emotional upsets.) The necrotic end of an artery that has bled is apparently jarred loose by emotions such as fright or being upset nervously, initiating the bleeding.

Summary and Conclusions

1. From 1935 to 1945, 5,210 women have consulted the gynecologic department of the University of Minnesota Student Health Service because of pain, vaginal discharge, and irregular uterine bleeding.

2. One thousand six hundred sixty-seven women, or 32 per cent, presented themselves because of irregular bleeding.

3. An accurate pelvic examination can be made with one finger bimanual and/or rectal examination.

4. Menorrheal irregularities are classified. Hormonal studies have been done on the urine in normal cases and on patients with cystic glandular hyperplasia, irregular shedding, and oligomenorrhea.

5. Opportunity to study the results of gonadotropic hormone administration can best be accomplished in an institution where the results can be better evaluated, and patient is saved the expense of hormone injections.

6. Abnormal uterine bleeding is frequently self-limited, and results due to spontaneous remissions or other fortuitous factors must be kept in mind before one judges the efficacy of any therapy.

7. X-ray therapy or radium have not been used in any of the students in this group.

8. Thyroid medication is probably still the best method of balancing the endocrine glands.

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A DIAGNOSTIC TECHNIQUE FOR THE DETECTION OF ENTEROCELE

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ENTEROCELE was formerly believed to be a surgical rarity. Considered opinion now regards its "rarity" as based on lack of detection rather than occurrence. High rectoceles and posthysterectomy rectoceles are more frequently true enteroceles, either undetected at operation or developing subsequent to (usually) supravaginal hysterectomy. Certainly it is seen too often to be considered other than a probable accompaniment of marked rectocele, or the sole cause for the posterior vaginal wall bulge when the latter extends high in the vagina. While gynecologists may be concerned with its existence and treatment, its nature and even name are foreign to most practitioners.

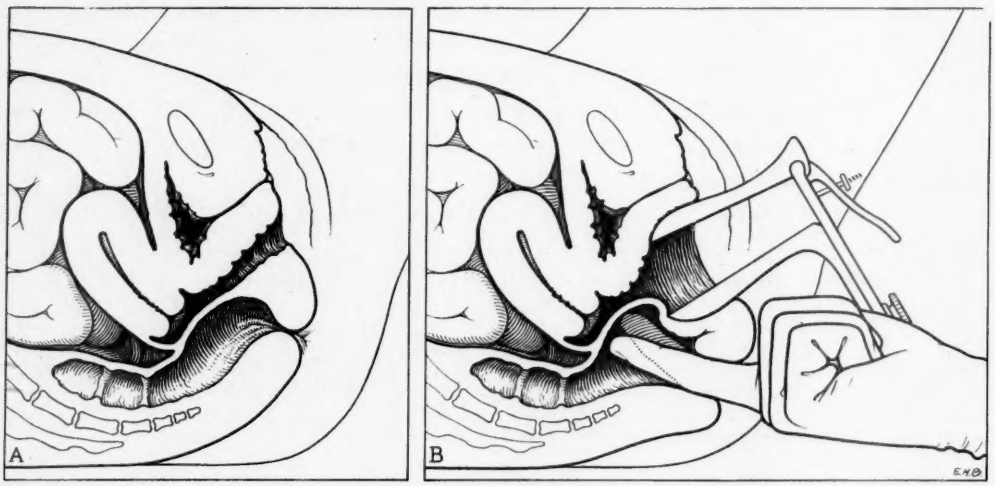

Fig. 1.—(*A*). Rectocele above firm perineal body. (*B*). Demonstrating rectocele. Withdrawal of speculum permits rectal wall to "fall away" from rectal finger, which follows into sacculated rectocele.

Since an enterocele must be recognized—usually *before* operation—to be eradicated *during* operation, not only must the awareness of its occurrence be cultivated, but also simple diagnostic steps taken to seek it out. It is rightfully regarded as a true hernia, for it is a saccular projection of the peritoneum of Douglas' cul-de-sac through a defect in the endopelvic fascia. This defect, either congenital or acquired, is between the uterosacral ligaments and opens the path for the peritoneal pouch protrusion into the areolar tissue between the enveloping fasciae of the rectum and the posterior vaginal wall. This herniation progresses until the structures of the inferior pelvic diaphragm (the perineal body) are encountered. It then may "roll over" these and present as a bulge at the introitus. In parous patients, the loss of anatomic semblance is confusing, for rectocele is a frequent complicating condition, and the coexistence of the two entities may be overlooked.

In proceeding to determine the nature of the protrusion of a posterior vaginal bulge, one must recall that an enterocele is dependent upon a fascial defect in the endopelvic fascia without necessarily any impairment in the enveloping fasciae of the vagina or rectum, whereas a rectocele is a hernia directly dependent for its development upon loss of the fascial support of the

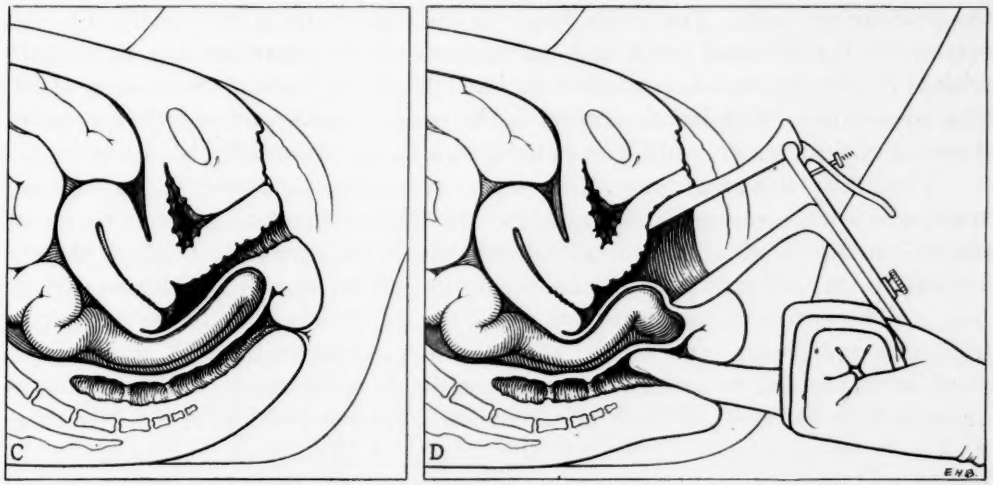

Fig. 2.—(*C*). Large enterocele without rectocele. (*D*). Demonstrating enterocele. On withdrawing the speculum the enterocele bulges into the vagina, but the rectal wall maintains contact with the rectal finger, for the enterocele separates and "fills" the rectovaginal septum.

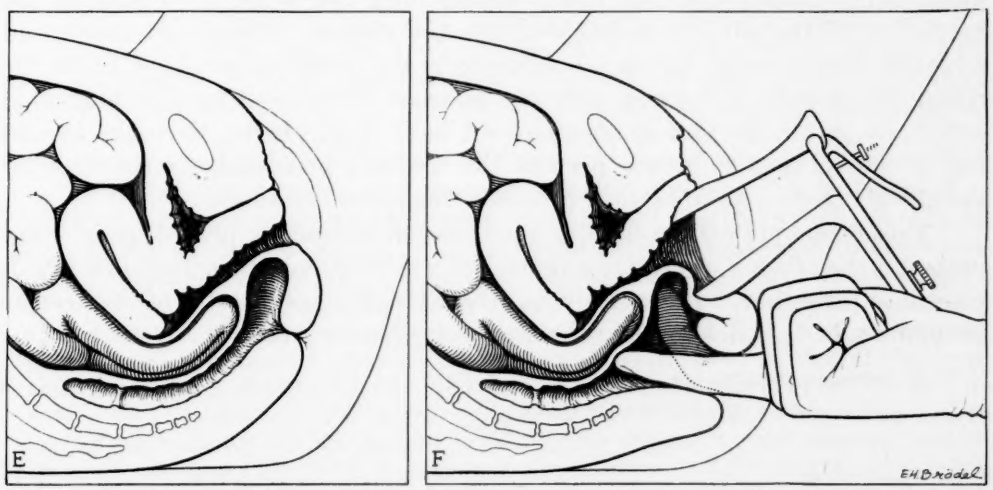

Fig. 3.—(*E*). Enterocele and rectocele. (*F*). Demonstrating enterocele and rectocele. As the speculum is withdrawn, the enterocele herniates into the vagina but the rectal wall maintains contact with the rectal finger, as in *D*. Further speculum withdrawal reaches the site of rectocele, and now the rectal wall falls forward away from the finger, which must flex to maintain contact, as in *B*.

posterior vaginal wall and rectum through injury of the fused levator and urogenital diaphragm fasciae. Since injury plays a large role in their evolution, the association is expected.

The common methods employed to diagnose enterocele are manual and speculum vaginal examination and rectal digital examination. In my opinion,

these are not always conclusive. However, the simple combination of concomitant vaginal-speculum and rectal-digital examination is positively diagnostic. At the conclusion of the usual gynecologic examination of a patient presenting a "rectocele" either independently or in association with coexisting pelvic pathology, a bivalve speculum (Graves or other) is introduced deeply into the vagina with the posterior blade exposing the cervix and restraining the postvaginal wall. The index finger of the right hand is introduced into the rectum to the cervical level and maintained with palmar surface in contact with the anterior rectal (posterior vaginal) walls throughout the examination. The speculum is withdrawn first with the patient quiescent and then reintroduced and withdrawn while the patient strains or "bears down" forcibly.

The three drawings show the pelvic relationships found in the normal state, and with enterocele and rectocele. In the normal state, there is no rectal bulge into the vagina as a bivalve speculum is withdrawn. With either enterocele or rectocele, although the herniation is obvious, especially on straining, a differential diagnosis is not possible. If, however, a finger is carried high into the rectum and placed against the anterior rectal wall, and the patient is instructed to strain as the speculum is withdrawn, the existence of enterocele or rectocele or both is immediately determined and accurately diagnosed. If an enterocele is present, the bulge into the vagina begins below the cervix and progressively enlarges to its lower extent, while the anterior rectal wall is held in contact with the rectal finger. In rectocele, the bulge occurs lower in the vagina and, as the speculum is withdrawn, the anterior rectal wall "falls" away from the rectal finger, since the bulge is formed by the herniation of the anterior rectal wall into the vagina. If both enterocele and rectocele are present, the two observations are noted in sequence, with the rectal finger held in contact with the anterior rectal wall by the interposed enterocele, until the site of the perineal body is reached. Here the loss of fascial and muscle structure permits the forward herniation of the anterior rectal wall (rectocele) *beneath* the already diagnosed enterocele.

This technique can be used as the terminal diagnostic procedure in every patient presenting a posterior vaginal wall relaxation. In actual practice it consumes little time, but conclusively determines the exact status of the herniae encountered. It is definitive in the diagnosis of enterocele.

39 Gifford Avenue

SULFONAMIDES AS A PROPHYLACTIC AGENT IN CONJUNCTION WITH CESAREAN SECTION

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AFTER the therapeutic value of sulfonamides was established, it was proposed that one or more of them might be used in a prophylactic fashion. Various reports have been given. The Army and Navy Medical Corps gave trials on prophylactic value for injuries sustained in combat and for venereal exposures. The purpose of this presentation is to give our observation on the deposition of sulfanilamide in forty patients and sulfathiazole in three patients under the peritoneal reflection from the urinary bladder to the uterus in association with the closures of the uterine wound at the time of cesarean section.

Techniques

Obviously, any reduction in puerperal febrile morbidity is most desirable. If the infection occurred along the incision or in traumatized tissue, then it might be prevented by the use of sulfonamides in these sites. Without any particular guide, a little exploration was attempted. At first, sulfonamides were placed in the uterine cavity with the routine intrauterine small pack. This pack was removed vaginally in eight hours. Not enough was absorbed to yield even a trace in the blood tests. Clotting occurred about the crystals, which likely made a complete barrier to absorption.

To confirm these first findings, sulfonamide powder was encased in a thin cloth sack and it was placed in the uterine cavity with the pack. A blood clot formed around the pack also. As nearly as could be determined, none of the sulfonamide had been removed. Since this exploration exposed the inadequacy of the free intrauterine application for prophylactic use, a direct application of sulfonamides to the incised uterine wall seemed appropriate for investigation.

Practically all of the cesarean sections at the Chicago Lying-in Hospital are performed by the laparotrachelotomy technique. This technique entails the detachment of the vesico-uterine peritoneum at its attachment to the uterus (just below the "white line") and the reflection downward of this peritoneal layer which then exposes the lower uterine segment. A sagittal incision is made through the lower segment wall in this exposed area, but occasionally the incision is extended upward beyond the "white line." The uterine wall incision is closed in two layers. The first by interrupted catgut suture and the second layer including the fascia by a continuous catgut stitch. The vesico-uterine peritoneum is reattached back to the uterus to its original site or above, if necessary, to cover completely the incision. Accordingly, this space, formerly composed of loose areolar tissue, was an area in which deposition of sulfonamide powder might have some value in preventing infection in the uterine incision or adjacent tissues, and yet not interfere with wound healing of uterine wall. It has been observed that direct spread of endometritis may pass rapidly through the incision.

Results

Sulfathiazole was employed in only a few instances, while sulfanilamide was used generally because it was available in commercially prepared sterile

packages. Table I gives the indications (toxemia, placenta previa and abruptio placentae, disproportion and dystocia, previous cesarean section, or miscellaneous) for the cesarean section, and correlated with it is the type of anesthetic in relation to febrile and afebrile convalescence. Febrile means that the patient had a temperature of 38° C. (100.4° F. or more) on two or more days, excluding the first postpartum day. The four groups of anesthesia for this and the other table are local, local and gas, gas, and caudal. In 10 patients that had cesarean section in which sulfonamides were placed within the uterine cavity, seven were afebrile, while three were febrile. Eight of these 10 patients had local anesthesia, and two had local and gas. A second group is composed of 15 patients who had Porro cesarean section in 1942 to 1943 (during the same time that the former group was observed). Of this number, 12, or 80 per cent, were afebrile.

TABLE I. INTRAUTERINE SULFONAMIDES IN CESAREAN SECTIONS AND PORRO SECTIONS DURING THE PERIOD OF THE STUDY

	INTRAUTERINE SULFONAMIDES 10 LAPARO-TRACHELOTOMIES		PORRO CESAREAN SECTIONS WITHOUT SULFONAMIDES	
	AFEBRILE 7	FEBRILE 3 (30%)	AFEBRILE 12	FEBRILE 3 (20%)
Toxemia	2	0	0	0
Placenta previa and abruptio	0	0	2	2
Disproportion and dystocia	3	2	1	0
Previous cesarean section	1	1	3	1
Miscellaneous	1	0	6	0
Local	6	2	0	0
Local and gas	1	1	2	2
Gas	0	0	8	1
Caudal	0	0	2	0

TABLE II. CESAREAN SECTIONS WITH AND WITHOUT SULFONAMIDES UNDER THE VESICO-UTERINE PERITONEUM

	SULFONAMIDES UNDER THE VESICO-UTERINE PERITONEUM		CONTROL GROUP OF 125 NO SULFONAMIDES	
	AFEBRILE 27 (63%)	FEBRILE 16 (37%)	AFEBRILE 90 (72%)	FEBRILE 35 (28%)
Toxemia	2	1 (33%)	11	6 (35%)
Placenta previa and abruptio	2	1 (33%)	14	8 (36%)
Disproportion and dystocia	8	10 (56%	29	13 (31%)
Previous cesarean section	13	4 (23%)	25	5 (17%)
Miscellaneous	2	0 (0%)	11	3 (21%)
Local	6	10 (63%)	50	15 (23%)
Local and gas	6	3 (33%)	14	5 (26%)
Gas	6	1 (14%)	22	12 (35%)
Caudal	9	2 (18%)	4	3 (43%)

For a control (untreated) group (Table II) of cesarean section, 125 unselected or uncorrected patients were chosen. Ninety, or 72 per cent, were afebrile, whereas 35, or 28 per cent, were febrile. This percentage is more statistically significant since the total number is large. Nevertheless, 72 per cent does not differ greatly from the 80 per cent when it is realized that there were but 15 patients in the other series. Febrile courses occurred in all five clinical divisions of toxemia, placenta previa and abruptio, disproportion and dystocia, previous cesarean section, and miscellaneous groups. Likewise, febrile courses followed all types of anesthesia.

The treated group consisted of 43 patients. The incision in the uterus was closed in the routine fashion. When the area covered by the detached

vesico-uterine peritoneum was free from blood and dry, 5 Gm. of sulfonamide powder was deposited over the uterine fascia. The peritoneum was reattached to the uterine wall, covering the sulfonamide powder. Special efforts were made to keep the sulfonamide within this zone and out of the free peritoneal cavity. In this group of 43 patients, 16 of them, or 37 per cent, were febrile. This is the highest febrile group in the entire series, in spite of the fact that an effort was under way to reduce or prevent a febrile course. Moreover, there was no evidence that the febrile reaction in any of these was on a basis of drug sensitization.

The cesarean sections were performed electively in several instances because of a previous cesarean section. It will be noted that the disproportion and dystocia group had 10 febrile to the eight afebrile. In the control group, local anesthesia was used more than all others, while in this limited series local anesthesias alone were not so dominant.

Richards[1] believes that local implantation should be beneficial, but his number of patients are too small to be conclusive. Anderson and associates[2] demonstrated that an intrauterine pack completely filling the uterus can be left in situ for a protracted period when the sulfonamides are impregnated or placed in the pack. We observed one patient who had a pack in the uterus for twelve days without febrile reaction. Because of a blood dyscrasia the pack was left for this time. Sulfathiazole was added to the pack and penicillin given hypodermically over this entire period. The small pack customarily employed in laparotrachelotomy could not compare to the tight pack for postpartum hemorrhage. Ramos[3] advances great claims for the use of sulfonamide therapy in a prophylactic manner at the time of cesarean section. Their number of untreated patients was 429, with a mortality of 4.89 per cent. There were 69 patients which they treated, with a mortality of 1.45 per cent. He did not discuss other therapies, as blood transfusion and improved techniques. The mortality rate of 4 per cent is entirely too high by the standards of the better maternities in the United States. Perhaps Ramos is dealing with a different type of patient than that which is encountered in the Chicago Lying-in Hospital.

Blood Levels

Hesseltine[4] reported blood levels on 32 patients (30 who had 5 Gm. sulfanilamide, and two who had 5 Gm. sulfathiazole). Readings were made at the fourth, eighth, twelfth, and twenty-fourth hours after the deposition. One test was made at the sixteenth and also twentieth hours.

The ranges for the two patients on sulfathiazole are:

Hr.	*4th*	*8th*	*24th*
Mg.	3.0	2.6	1.9
Mg.	1.0	--	--

The thirty on sulfanilamide had ranges at fourth, eighth, twelfth, and twenty-fourth hours as follows:

Hr.	*4th*	*8th*	*12th*	*24th*
Highest	10.8	10.0	6.9	6.7
Lowest	1.0	1.8	2.0	1.5

The average of the sulfonamide levels are:

Hr.	*4th*	*8th*	*12th*	*24th*
	3.3	4.0	3.8	3.0

This indicates that good absorption can be expected from this site. However, rates are so erratic and unpredictable that this is an unsatisfactory channel for establishing effective and dependable levels.

Conclusions

From these observations, it is evident that the use of sulfonamide locally did not lower the morbidity rate nor shorten convalescence. Furthermore, the bladder peritoneum seemed more adherent in a few patients subjected to laparotomy subsequently. This may not be serious, but it requires greater caution in the reflection of this tissue in subsequent laparotrachelotomies.

Therefore, the local deposition of sulfonamides, either within the uterine cavity or over the uterine incision (but under the peritoneal reflection) did not reveal any prophylactic value. It did increase adhesions of the peritoneum to the uterus. There exists also the dangers of drug sensitization.

The sulfonamides in relation to cesarean section should be used on direct indication in relation to a proper bacteriologic study of the uterine cavity and blood stream, except in such urgent situations where the withholding of the drug would jeopardize the patient's convalescence or life. Even in this event today penicillin would seem preferable to the sulfonamides with but few exceptions. Penicillin, like any other medicament, should be employed in sufficient and proper dosage and only when properly indicated.

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ACUTE POSTPARTUM NECROSIS OF THE ANTERIOR HYPOPHYSIS

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WE HAVE recently (publication of case delayed by military service) had experience with a case of acute postpartum necrosis of the anterior hypophysis, wherein the patient exhibited spontaneous hypoglycemia of a severe degree and survived the acute episode long enough to display some of the manifestations of Simmonds' disease. Because of the infrequency of cases wherein the clinical diagnosis has been made, followed by a temporary recovery, subsequent death, and autopsy, we desire to report this case in some detail.

Much confusion is apparent in the present-day literature regarding the physiology of the anterior pituitary, but some light is being brought into the picture by the increasing attention to destructive lesions of the anterior lobe, following shock at delivery, resulting in the clinical picture of Simmonds' disease. In 1883, Simpson[1] described the syndrome, described the clinical course, and mentioned etiologic factors, but it was not until 1914 that Simmonds[2] described the pathology of the disease that bears his name. Maresch,[3] in the same year, called attention to the fact that hypopituitarism was likely to occur in patients who experienced repeated labors, especially when accompanied by hemorrhage. He maintained that those cases represented functional exhaustion of the pituitary gland. Silver,[4] in 1933, reported that in 26 out of 39 autopsies on cases of Simmonds' disease there was atrophy or fibrosis of the anterior pituitary. He explained the etiology of this pathologic picture by assuming embolism of the pituitary vessels, as a result of puerperal sepsis.

The recent work of Sheehan[5-8] and Murdoch has shown conclusively the close relationship between postpartum necrosis and shock and hemorrhage at delivery. Since the work of these investigators, isolated reports have appeared in the literature. In 1942, Escamilla[9] and Lisser presented the most complete review and analysis of the literature to date. They collected data on 595 cases suggestive of Simmonds' disease in one form or another. This valuable material was gathered from a thorough search of the literature, personal communications, and their own cases. All cases were subjected to critical analysis regarding etiology, symptomatology, and treatment. According to their study, there had been until that date 27 cases of Simmonds' disease, upon which autopsies had been performed, and the etiology established as originating from massive necrosis of the anterior hypophysis, accompanying collapse or hemorrhage at delivery.

Case Report

Mrs. L. V., a 32-year-old white primigravida, was admitted to the Charity Hospital on April 11, 1942, having generalized convulsions. The last normal menstrual period had been on July 4, 1941, and the patient had been under a physician's care since the sixth week of pregnancy. At the third month she

had manifested slight albuminuria, but, according to her doctor's report, this had cleared up in a short time. The course of pregnancy was then uneventful until one month before admission when there was a return of albuminuria and, for the first time, hypertension was observed (140/90). There was a weight gain of 28 pounds during the entire course of pregnancy. When hospitalization was advised because of the signs of toxemia, the patient refused, and during the ensuing four weeks hypertension continued, accompanied by headaches and pedal edema. On the day prior to admission, the patient exhibited restlessness and epigastric pain, followed by a generalized convulsion on the morning of admission. The convulsion lasted ten minutes, followed by unconsciousness; she was then admitted to the hospital.

Review of the past history was void for scarlet fever, nephritis, pyelitis, hypertension, or contagious diseases. Menses began at 18 years of age and were accompanied by severe occipital headaches throughout her adult life. Both the patient and her robust brother give a history of fainting upon slight provocation, especially with emotional excitement. There was vomiting during the first trimester, with return of that symptom two weeks prior to admission.

On admission, the patient was observed to be obviously in the third trimester of pregnancy, having generalized tonic and clonic convulsions (apparently the second seizure). Her temperature was 98.6° F., pulse 145, respiration 30, and blood pressure 207/160. Examination of the eye grounds revealed bilateral peripapillary edema, numerous points of A-V notching, without great disproportion in the A/V ratio. One flame-shaped hemorrhage was noted. Examination of the chest revealed gallop cardiac rhythm and moist pulmonary rales at both lung bases. Edema of the extremities was described as slight. Other than the obstetric findings (eight to eight and one-half months pregnancy, not in labor, vertex presentation, normal fetal heart tones) the remainder of the physical examination was negative.

The following laboratory data were obtained on admission: *Urine:* albumin 65 per cent moist (Purdy); sugar: negative; sediment: 10 red blood cells, 20 white blood cells, few hyaline casts (high power field). *Blood Chemistry:* carbon dioxide, 22; urea, 16.7; glucose, 87. *Venous Pressure:* 175 mm. H_2O.

Eclampsia was handled by the usual methods of dehydration and sedation. No further convulsions were experienced. Onset of labor was spontaneous, and delivery was accomplished by low forceps and episiotomy under local analgesia the following afternoon. Blood loss at delivery was estimated at 400 c.c. Blood pressure prior to delivery was 150/100, but by the conclusion of the delivery it had fallen to 78/50, although delivery was accomplished without difficulty and the third stage was entirely normal. Shock was treated by transfusions of citrated blood and pooled plasma, without effect on the blood pressure. Two doses of adrenalin intravenously were required to elevate the blood pressure above shock level, after which it became stabilized at 90 to 100 systolic. It was estimated that the blood pressure remained at severe shock level for about one and one-half hours and at mild shock level for about nine hours, during which time 4 c.c. of Eschatin were given intravenously. The pulse rate remained at 132 for eighteen hours. Because of very poor urinary output during the first twenty-four hours after delivery, diathermy was given over the kidney areas and hypertonic glucose was administered in large quantities, intravenously, with Ringer's lactate solution to combat the acidosis. Improvement was slow, but by the fourth hospital day, the urinary output had reached 700 c.c. for a twelve-hour period.

Because of a marked anemia, on the seventh hospital day the patient was given a transfusion of 500 c.c. of citrated blood. By error this was followed by a liter of distilled water. Before the error was detected, the entire infusion had drained and the patient complained of generalized aching, had several

loose stools, and became stuporous. The blood pressure rose to 180/110, the rectal temperature dropped to 95° F., and mucus accumulated in the throat. Twelve hours later the patient was in a moribund condition. Because of acidosis, and the clinical impression of hypoglycemia, 300 c.c. of 5 per cent soda bicarbonate followed by 50 c.c. of 50 per cent glucose was administered intravenously. Within thirty minutes there was a dramatic change in the patient's condition. She was relieved of coma, appeared alert, responded to questions, and was able to supply missing details in her past history. An infusion of 1,000 c.c. of 10 per cent glucose was then given. It was noted here (as it had been on the day after admission), that despite administration of large quantities of glucose intravenously, *no glucose spilled over into the urine nor was there any appreciable rise in the blood sugar.* That evening the patient again required administration of 50 per cent glucose intravenously to combat a relapse into a semicomatose state. Again, the response was dramatic. Blood chemistry taken after response showed: nonprotein nitrogen, 30; glucose, 104; carbon dioxide, 48.

The following morning the blood chemistry showed: urea, 61; glucose, 62; carbon dioxide, 44; serum proteins, 5.11. A continuous drip of hypertonic glucose was given throughout the day, and administration of adrenalin min. V raised the blood pressure to 190/90, but failed to produce a rise in the blood sugar level, or promote glycosuria, despite the infusion.

On the ninth day, despite continuous administration of 20 per cent glucose by intravenous drip, the patient became comatose, requiring 50 per cent glucose to relieve the coma. It was then decided that in all probability the case was one of pituitary necrosis, so whole antuitrin therapy was begun. No effect was observed after twelve hours, during which time 11 c.c. was administered, so this therapy was abandoned.

The following day, desoxycorticosterone acetate therapy, in conjunction with regulated sodium chloride administration, was started. Twenty mg. of DOCA was given in the first twenty-four hours, with a maintenance dose of 15 mg. day thereafter. One liter of normal saline was allowed per twenty-four hours. At this time, the nonprotein nitrogen was 75; urea, 52; creatinine, 9.7; glucose, 64; plasma chlorides, 445; carbon dioxide combining power, 44. Another transfusion was given, without incident, and improvement seemed to follow. The urea nitrogen fell to 48, and the glucose rose to 85. The patient remained rational, and apparently the DOCA was achieving its purpose, because 50 per cent glucose was no longer required, although hypertonic glucose infusions were continued for a few days.

It was noted that lactation had never occurred and that the breasts were very small. Urinary output at this time was excellent. On the thirteenth day the patient's condition was good, and infusions were discontinued. Blood Chemistry: urea, 50; creatinine, 7; glucose, 64; chlorides, 574. It was noted here that, although there was not much apparent improvement in the blood chemistry findings, still, definite improvement was reflected because these were interpreted as true values, whereas previous specimens were considered to have been greatly diluted, because of the continuous infusions.

When it was attempted to reduce the dose of DOCA, within twenty-four hours the patient relapsed into a comatose state, with mild convulsions. Blood glucose was reported as 48. Rectal temperature was 95° F. With administration of glucose and increased dosage of DOCA (5 mg. every six hours, rather than every twelve hours) the patient's condition again rapidly improved.

The basal metabolism rate was determined and found to be −31. It was noticed that brownish pigmentation, previously noted, seemed to be increasing, especially over the arms. X-ray of the chest revealed no disturbance of the cardiothoracic ratio.

On the fifteenth hospital day, the patient was able to sit up in a chair all day, and visit her baby in the nursery. Blood chemistry on this day: urea, 59; creatinine, 5.5; glucose, 58; chlorides, 445. Two days later, the patient developed signs of a thrombophlebitis (secondary to glucose administrations) in the right saphenous vein. The following day the saphenous and femoral veins on that side were ligated, followed by lumbar sympathetic block. During the next few days the patient ran a septic course and the general condition became worse. Urinary output diminished, and pyuria became marked.

Fig. 1.—Enlarged photograph of sectioned pituitary gland, showing massive necrosis of anterior lobe.

Fig. 2.—Photomicrograph of necrotic area of anterior pituitary, showing a few glandular elements at periphery.

With general supportive therapy, the condition again improved, and on May 3 (22nd hospital day) thyroid therapy was started. Two days later the patient relapsed and again the septic picture became pronounced. On May 7, generalized maculopapular spots appeared, and blood culture was reported as positive for *Staphylococcus albus*. Blood chemistry: urea, 108; creatinine, 10.5; sugar, 266; chlorides, 515 (infusions had been discontinued, fluid intake was very poor, and this was interpreted as being very concentrated). Repeated blood cultures continued positive for *Staph. albus*, and, despite heroic measures, the patient died on May 11.

Autopsy performed immediately following death revealed the following: *Pituitary:* weight: 0.506 Gm. In the anterior lobe there was a yellow depressed

area replacing about 85 per cent of the gland substance. Microscopically, practically the entire anterior lobe stained pink, without any cellular details. Only a few pyknotic remnants of nuclei were noted. Adjacent to the pars intermedia, a few acini were noted. The blood vessels showed thrombosis and occlusion. The posterior lobe was normal (Figs. 1 and 2). *Breast:* the acini and ducts were small and greatly separated by a large amount of adipose tissue. *Ovaries:* no Graafian follicles or corpora lutea were noted. *Uterus:* no endometrium was noted. *Adrenals:* grossly normal. Microscopically, the cells of the reticular and fasicular layers were highly vacuolated. The medullary cells stained darker than usual. *Lungs:* on the right there was a subpleural abscess, with apical pulmonary fibrosis. *Pancreas:* the pancreas weighed 100 Gm., and showed no gross or microscopic pathology other than an increased amount of loose fibrous tissue surrounding acini, ducts, and islets. *Kidneys:* right 100 Gm., left 135 Gm. The right kidney lay in the midline, adjacent to L4. It had a bizarre shape, and presented no definite hilum. Vessels entered at the superior pole. Ureter left the kidney from three sites. Capsules of both kidneys stripped with difficulty. There was indistinct demarcation between the cortex and medulla. Calices and pelvis of the left kidney were normal. The right renal artery and vein arose just above the bifurcation of the aorta and inferior vena cava, respectively. Microscopically, there was dilatation of the tubules and Bowman's spaces. In the interstitial tissues there were collections of polys and macrophages. *Right Femoral Vein:* firm gray blood clot 3 cm. long, extending into the external iliac vein.

Discussion

The patient in whom postpartum necrosis of the anterior pituitary occurred may die early in the puerperium, either as a result of obstetric shock, or of the necrosis per se. In this instance, localizing symptoms and signs are difficult to define, and diagnosis may rest upon empiricism, if death occurs before fourteen hours have elapsed, examination of the pituitary will fail to reveal the lesion.

On the other hand, if the patient survives the immediate crisis, the clinical picture is distinct, although variable, and dependent upon the proportion of gland substance destroyed. Sheehan emphasizes the quantitative aspect of Simmonds' disease. It has been shown that patients may exhibit no symptoms following destruction of 50 per cent of the anterior lobe, while destruction of 75 per cent will give rise to moderate symptoms, and only with destruction of 90 per cent of the gland substance will severe clinical symptoms be given.

In the early puerperium, the only localizing signs are the inhibition of lactation, and occasionally hypoglycemia, later a characteristic pattern of signs and symptoms appear, depending upon the degree of pituitary damage. Amenorrhea, hypometabolism, hypoglycemia, hypopiesia, anemia, loss of body hair, apathy, asthenia, progyria, and occasionally, but terminally, cachexia are noteworthy manifestations of this condition.

The exact mechanism whereby pituitary necrosis is produced is unknown. Several factors conducive to the development of this strange phenomenon have long been known: (1) Hyperplasia of the pituitary during pregnancy; (2) the rigid bony cage enclosing the gland, resisting the hypertrophy; (3) sinusoidal arrangement of the blood vessels in the parenchyma. Incongrously we must admit the very rich blood supply afforded by the circle of Willis. The initiating mechanism, at any rate, begins with collapse from shock or hemorrhage at

delivery. It has been suggested that there is thrombosis of the pituitary vessels, but this has never been shown consistently at autopsy. More likely, associated with general collapse, there is collapse of the vessels and sinusoids in the gland itself. If prolonged, this could, in itself, produce the typical picture of ischemic necrosis. However, stagnation and physiochemical changes in the blood might conceivably account for the small thromboses seen in the smaller vessels, within the gland substance, and the theory of thrombosis seem to hold. In any event, microscopic examination of the necrotic area always gives the typical appearance of ischemic necrosis—infarction. Various authors (Silver, Riecker, Curtiss) emphasize the importance of puerperal sepsis, and attribute the necrosis to embolic phenomena. It is the opinion of most authors, however, that sepsis plays a minor role in most cases.

Treatment

The results of treatment, to date, have been so discouraging that prophylaxis bears more emphasis. Improved obstetrics, proper prenatal supervision, careful conduct of the third stage, and the judicious management of the complications of pregnancy, especially those which predispose to hemorrhage and collapse, are of utmost importance. Preliminary blood matching and "Rh" determination of "dangerous cases," vigilant observation for the early signs of shock, and the prompt, or better, prophylactic administration of blood and/or plasma assume an even greater obstetric significance in the light of pituitary necrosis. Sheehan has shown that 25 per cent of patients suffering collapse at delivery subsequently exhibit evidence of Simmonds' disease.

Second in importance to prophylaxis is early diagnosis. This often must depend upon suspicion, or realization of the fact that conditions are present for the development of this complication. Treatment of the developed condition may be considered under two headings: early, and late. Early treatment is directed toward relieving shock, replacing blood loss, and correction of the obstetric situation which precipitated shock. The blood chemistry should be studied early and frequently. Hypoglycemia should be prevented, as many of these cases die in coma, undoubtedly associated with a hypoglycemic state. Secondary collapse or hemorrhage must be prevented, once the acute episode is controlled.

Unfortunately, most of the discussions of treatment in the literature are concerned with the therapy of Simmonds' disease, or the late effects of the necrosis, and little is offered in the management of the acutely developed condition. It has been shown in animal study that total hypophysectomy need not be followed by death. We have been able to locate only one article relating a human case report, and in this instance the gland had slowly lost its function by the development of a tumor. This patient was alive three years after total hypophysectomy, but demonstrated osteogenic effects and fairly constant hypoglycemia. We know of no instance where a patient survived the extirpation of an entirely normal pituitary gland. It seems likely, however, that such would be possible, because, in many of the cases of severe Simmonds' disease, postmortem examination years later has shown almost

complete destruction of the anterior hypophysis. Be that as it may, extensive necrosis is a major shock to the normal physiology, and some sort of substitution therapy should be attempted.

1. *Pituitary Extracts.*—There are reports of success following the use of various extracts of whole anterior pituitary substance. This line of therapy is entirely rational, but, unfortunately, feeble. The available extracts are of uncertain potency, as there is no chemical or biologic standardization. The only thing certain is their impotence, and it may be stated that they fall in the general category of "endocrine soups." In the future, with improved chemical methods, much is to be expected from this line of therapy, but for the present we must rely largely upon other therapeutic weapons.

2. *Glucose.*—Glucose is invaluable in those cases exhibiting disturbed carbohydrate metabolism, but it must be remembered that tolerance to glucose will increase until functional exhaustion of the islets of the pancreas occurs. Then diabetic failure will supervene. Nevertheless, concentrated glucose should be employed generously until carbohydrate metabolism can be regulated. As well shown by this case, one must be more than attentive to the veins of patients receiving hypertonic glucose, because, while the glucose may be life-saving, the administration may indirectly cause the death of the patient as a result of phlebitis and septicemia.

3. *Adrenal Extracts.*—Because of the rather acute adrenal failure secondary to removal of pituitary stimulation, attention must be given to replacement therapy until such time as pituitary function can be restored or replaced. While pathologic changes in the adrenals have been consistently reported, there is no reason to assume primary adrenal damage, so that replacement therapy is dependent upon absence of pituitary stimulation.

There are no hard and fast rules governing the dosages of adrenal extracts in the acute crisis. Empiricism must be practiced at first and, after balance has been established, the general rules applied in most cases of Addison's disease may be followed, depending upon the severity of the case. It must be remembered, however, that just as in Addison's disease, potassium restriction is just as necessary as sodium administration.

In the treatment of acute cortical deficiency, most authors agree that the administration of whole cortical extract is preferable to the use of desoxycorticosterone acetate. Kendall[10] has listed eleven steroids of known formulae, in the corticosterone group. In addition to these, the adrenal cortex is known to contain desoxycorticosterone, progesterone, estrone, and certain androgens.[11] Of special significance are the steroids designated by Kendall as Compounds A, B, E, and F. These four steroids all contain an oxygen atom on C11, which desoxycorticosterone does not, and this is of importance in carbohydrate metabolism. Kendall[12] credits the ketol structure on C 17 for enabling the cortical hormones to maintain life in the adrenalectomized animal. Progesterone possesses such a group, and has been shown to be capable of prolonging life in the adrenalectomized animal.[11]

It is interesting to note that, despite the isolation of so many chemically pure steroids from the adrenal cortex, the mother liquor from which they are

prepared still retains the major portion of the total activity of the crude extract. The chemically impure amorphous substance remaining in the mother liquor has been shown to be capable of maintaining life in the adrenalectomized dog in $\frac{1}{15}$ of the amount required of DOC and $\frac{1}{100}$ the amount required by corticosterone.[13]

For glucogenesis, corticosterone, compound E, and their derivatives with oxygen on C11 are necessary, whereas DOC appears to have the most marked effect on the distribution of electrolytes. For the maintenance of normal adrenal function, the amorphous fraction is most efficient.[14] It has been stated[11] that carbohydrate metabolism is somewhat dependent upon electrolyte and water balance, as shown by the fact that adrenalectomized animals can be maintained with regards to blood sugar and liver glycogen, on a diet high in salt and water, even in the absence of adrenal cortical hormone. However, these animals are peculiarly susceptible to stress, and even mild stimuli may precipitate against insulin in the insulin-sensitive adrenalectomized animal.[11] It has been shown that adrenalectomized animals have lowered resistance to toxins and infections. There is an appreciable decrease in antibody formation, and the whole defensive mechanism seems to be less responsive after adrenalectomy.

Hartman reported a lactation factor,[15] which enabled female rats to lactate in the presence of adrenal insufficiency. Compound E is also said to be effective in promoting lactation.

In planning cortical replacement therapy, one is confronted with the problem of substituting control of two widely different functions of the adrenal cortex, namely the maintenance of normal water and electrolyte balance, and the regulation of carbohydrate metabolism. The changes relative to disturbed water and electrolyte metabolism may be relieved by DOC; those related to carbohydrate metabolism may be remedied by whole cortical extract, or the corticosterone series, compounds A, B, E, and F of Kendall.

4. *Anterior Pituitary-like Hormones.*—Some success has been reported with the use of progesterone. This is easily understood, in the light of the above.

5. *Thyroid.*—While Sheehan[7] has contended that the use of thyroid extracts may be dangerous, he reports good results in the myxedematous type of patients. On the other hand, J. H. Means[16] has shown that it is exactly this type of patient that presents the real danger in employing thyroid therapy. The complication most to be feared is the development of sudden adrenal cortical failure. To prevent this, Means recommends high salt intake and anterior lobe extracts. He reports two cases of pituitary failure, associated with myxedema, treated by thyroid extract. The first patient died, showing true Simmonds's disease with diffuse fibrosis of the anterior pituitary. The other patient was rescued by salt therapy. The patient we have presented was apparently made worse by thyroid therapy.

6. *Pregnancy.*—Sheehan[7] has suggested that the most promising hope in a case of Simmonds' disease resulting from pituitary necrosis is the occurrence of another pregnancy. It appears that in nearly every instance where another pregnancy ensued, there was clinical cure, or marked remission of the symp-

toms, beginning in the early weeks. However, one of his cases experienced the almost unbelievable complication of another, a second pituitary necrosis in the subsequent pregnancy, and this was clearly demonstrated at autopsy. The physiologic hyperplasia of the pituitary during pregnancy, is, of course, the underlying basis for the improvement in his cases, and this leads to two interesting speculations. First, how is one to enhance the chances of pregnancy in a woman with Simmonds' disease, when the possibilities are so very poor, by the very nature of the disease? Second, what is the cause of the physiologic hyperplasia of the pituitary in pregnancy? While the latter might seem a very elementary question, because of its very simplicity it seems to have eluded solution. When the answer to this second question is known, the problem of replacement therapy may be approached on a much more rational basis.

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PROLAPSE OF THE UMBILICAL CORD

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OUR attention was drawn to the study of this unfortunate accident of labor because of an unusual grouping of cases which followed one another with alarming rapidity, and because of dissatisfaction with the results of our treatment. Survey of the literature did not help us to define the problem and formulate its solution, for we encountered frequent acceptance of types of treatment which were obviously unsuccessful and at times outmoded by recent obstetric advances. We were therefore led to a study of 71 cases of prolapsed cord which had occurred in our hospital during the period of ten years prior to this analysis. Our incidence approximated the 0.42 per cent reported by Bourgeois[6] in 1941.

Etiology.—In seeking etiologic factors we studied parity, presentation, and pelvic type with the following findings:

1. *Parity:* There were 29 primiparas in our group. This does not allow any conclusions regarding the significance of parity as an etiologic factor in our cases. Mengert and Longwell[5] have stressed the dangers of operative delivery in this group, for they found the fetal mortality in primigravidas almost twice that of multiparas. This is a significant consideration.

2. *Presentation:* We have encountered a similar preponderance of abnormal presentations to that reported by others.[1-4] Our series includes:

Vertex	30		
Breech	20		
Transverse	7		
Compound	1		
Twins	13—of these twins:		
		Vertex	14
		Breech	9
		Transverse	2
		Compound	1

This incidence is understandable, for the presentation other than vertex makes the cord more likely to prolapse through the unfilled lower uterine segment.

3. *Pelvis:* We have not found a high percentage of contracted pelves. In our group of 71 cases, the pelves were classified (clinically for the most part) as follows:

Gynecoid	51
Android	8
Anthropoid	9
Flat	3

In the entire group 65 were considered adequate for labor; six were considered small. This does not indicate that bony dystocia was an important element. It is in accord with the observations of Bourgeois, who believed other manipulative or accidental factors to be more important etiologically. He stressed the dangers in this regard of bagging or manual rotation of high heads, and also such accidents ase premature rupture of the membranes and increased

pressure incidental to struggling under anesthesia. Mengert and Longwell were of the opinion that premature rupture of the membranes was less important than length of cord.

It is evident in general that many factors, whose incidence and onset are uncontrollable, play an important etiologic role in prolapse of the umbilical cord. Therefore, early recognition and prompt efficient treatment are necessary to meet this problem. It is of interest to point out here that there were seven cases of *cord presentation* during this same ten-year period of study and to note that there were no fetal deaths in this group. Of these seven cases, three were discovered on the delivery table when the cervix was fully dilated and the patient ready for delivery, while four were discovered during a pelvic examination which was performed for failure to progress, irregularity of fetal heart, or unduly high station of the fetal heal.

Fetal Survival.—Fetal salvage was poor. In our group was noted:

Total babies who died	28 (39 per cent)
Viable babies who died	23 (32 per cent)

Breakdown of this fetal mortality reveals the major significance of the degree of cervical dilatation at the time of prolapse.

TABLE I. FETAL SURVIVAL

	LIVE BABIES	DEAD BABIES
Cervix fully dilated (or almost dilated)	36	9
Incomplete dilatation of cervix	7	19

It is obvious that the time factor and ease of prompt delivery were most important in securing a living child. It is of interest, therefore, to further study treatment of individual cases in two groups:

1. The group where dead babies were obtained in spite of full cervical dilatation: failure under relatively favorable conditions.

2. The group where live babies were obtained in spite of incomplete cervical dilatation: success under relatively unfavorable conditions.

It is obvious that in each of these instances the baby's condition before treatment of the prolapsed cord was so compromised or unpromising that no better result could be expected of any form of delivery.

This heterogeneous group permits no conclusions other than the recognition that good fortune may occasionally intervene when good judgment is lacking.

TABLE II. FULL CERVICAL DILATATION—DEAD BABIES

CASE NUMBER	TREATMENT	CONDITION OF BABY
2	Immediate breech extraction	Poor condition before treatment
24	Cord replaced; delivery with fundal pressure	Nonviable infant
25	Assisted breech	Nonviable infant
27	Pituitrin—spontaneous delivery	Nonviable infant
45	Immediate version and breech extraction	Poor condition before treatment
52	Immediate version and breech extraction	Poor condition before treatment
57	Cord replaced; attempted forceps at home (11½ lb. baby), later forceps extraction in hospital	Baby died before successful forceps delivery
63	Cord replaced; internal cephalic version and spontaneous delivery	Nonviable infant
64	Version and breech extraction; difficult operation for transverse presentation in tonic uterus	Infant probably dead before treatment

TABLE III. INCOMPLETE CERVICAL DILATATION—LIVE BABIES

CASE NUMBER	TREATMENT
6	Cord replaced; bagging; version and extraction
10	Full dilatation allowed; version and extraction
42	Manual dilatation; version and extraction
60	Full dilatation allowed; spontaneous breech delivery
62	Attempt at replacement and bagging; cesarean section
69	Cesarean section
70	Dührssen's incision; breech extraction

In breaking down the other group of failures, the instances of incomplete cervical dilatation where the infants did not survive, one first encounters eight of these 19 cases where the infant was either nonviable or in such poor condition before treatment was attempted that survival was unlikely. For the rest, attempts at cord replacement, Braxton-Hicks version, or expectant treatment were all attended by a notable lack of success. Furthermore, this group harbored the two maternal deaths in the series: No. 31 died of cervical laceration, hemorrhage, and shock initiated by attempts at manual dilatation of the cervix and breech extraction—moreover, this operation was attempted in the face of known intrapartum death of the child; No. 49 died of peritonitis resulting from rupture of a lymphogranulomatous rectal stricture—this was incurred during bagging and later breech extraction of a dead fetus.

Conclusions and Recommendations

1. As in other serious disorders where treatment is difficult, early recognition is most important. We therefore advise: (a) prompt pelvic examination when the fetal heart indicates fetal distress; (b) scrupulous attention to the time of rupture of the membranes in breech and transverse presentations and multiple pregnancies; immediate pelvic examination unless contraindicated.

2. Successful outcome is to be anticipated with full cervical dilatation by the use of the appropriate obstetric operation: forceps delivery, breech extraction, or version and extraction, carried out promptly but without undue haste. It is wise to allow fetal recovery from anoxia (after elevation of presenting part) before attempting delivery.

3. Improvement in results with incomplete cervical dilatation might be obtained by pursuing the following policy: (a) with recognition of a prolapsed cord, the patient should be transferred to a delivery room table, placed in combination lithotomy Trendelenburg position, anesthetized with oxygen-ether by a trained anesthetist, and examined under sterile conditions. (b) the examiner should lift the presenting part out of the inlet in an effort to relieve pressure on the cord. (c) if the fetal heart returns to normal and if the patient is primiparous, or the cervix less than 3F dilated, the patient should be subjected to cesarean section. While preparations for operation and induction of full anesthesia are completed, the examiner should continue to hold the presenting part out of the pelvis; the fetal heart should be checked repeatedly. (d) If the patient is multiparous and the cervix is 3 or more fingerbreadths dilated, it may be possible to secure safe operative dilatation by the use of the dilating bag. This of course calls for prior replacement of the cord which will be possible only with lesser degrees of cord prolapse.

4. If the infant has already succumbed at the time of recognition of the cord prolapse or it has been so badly compromised that the fetal heart cannot be improved with oxygen and elevation, it is unprofitable to subject the mother to major obstetric operations.

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THE TREATMENT OF ACUTE POSTPARTUM THROMBOPHLEBITIS OF THE LOWER EXTREMITY BY CONTINUOUS CAUDAL ANESTHESIA

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THE treatment of thrombophlebitis of the lower extremity is one of the most time-consuming and discouraging therapeutic measures attempted, particularly when handled by the traditional regimen of rest, elevation of the affected part, heat, and sedation. Heparin, dicumarin, penicillin, and sulfonamides are expensive, difficult of administration, dependent upon laboratory studies and control, or are only adjuvants to the so-called "conservative" or supportive treatment. However, if vascular inadequacy has become established, these medicaments will be of little or no value, and a confinement of six to eight weeks in bed followed often by years of swelling, pain, and disability confronts the patient.

Phlegmasia alba dolens, "milk-leg," or, more properly, postpartum femeroiliac thrombophlebitis is a catastrophy of the puerperium, and although much has been done in the prophylaxis of this complication, less has been accomplished in its treatment.

It is not within the scope of this paper to discuss all the causes of acute femoroiliac or femorosaphenous thromphlebitis, nor are we concerned primarily with their prophylaxis or diagnosis here, important though they may be. Moreover, although it is recognized that not all early cases are clear-cut, that the complete, typical findings are not invariably seen, and that a phlebothrombosis must be ruled out, we shall consider only the therapy of definite, acute postpartum infectious vascular occlusion of the venous system of the leg by continuous caudal anesthesia.

Pathologic Physiology of Thrombophlebitis

In 1934, Leriche and Kunlin[1] promulgated a theory of vasospasm in and about a vessel involved in a thrombophlebitic process. The vasomotor reflex, they indicated, originated in the irritated segment, involving the central nervous system, with a resulting upset of the normal intervascular relations. There were three phases involved in this process: (1) vasospasm—constant and most significant, (2) extension of the thrombus, and (3) arteriospasm. Leriche and others[2-4] reported numerous cases of thrombophlebitis all relieved by sympathetic nerve block following paravertebral injection of local anesthetics.

The development of the manifestations of thrombophlebitis, therefore, was on a basis of disturbed physiology, in a very large measure, rather than on an anatomic-pathologic foundation.

In 1939, Ochsner and DeBakey[5, 6] reported studies tending to prove that the evidence of pathology in the affected limb was not due to vasospasm so

much as to arteriospasm, and that in some cases no inflammation or infection was apparent. In these latter cases, phlebothrombosis was the term employed.

Spasm, in thrombophlebitis, is a major cause of pain and edema. The normal passage of fluids from each capillary loop into the tissues is from the arteriole end, whereas, the return of the extracellular fluid into the vasculature, excluding the lymphatics, is via the venule end of the loop.

In the spastic vasculature of a thrombophlebitic extremity, the blood flow is diminished, the endothelium of the capillaries is altered by hypoxia and the excess catabolic products, and the permeability of the vascular walls is increased. Exudation of fluid occurs at this point and a collection of intercellular, perivascular edema fluid is the result. The resorption of this excess fluid is difficult, for the arterial pressure in the extremity is lowered, the venous pressure is increased, and the pumping effect of the arterial pulsation is minimized in a spastic system.[5-7]

Sympathetic nerve block not only relieves the vascular spasm but also the pain, and allows collateral circulation to become effective.

This greatly diminishes the permeability of the capillaries, markedly reduces the probability of the extension of the thrombus, relieves back stasis and facilitates the natural processes of resolution and repair.

Ochsner and his associates[7] popularized the paravertebral lumbar sympathetic nerve block in the treatment of cases of thrombophlebitis. After insertion of three to five needles and the injection of an anesthetic agent into the paravertebral space opposite L.1-5, complete relief of pain held for about one to two hours, and the leg became flushed, warm, and dry. Although complete relief of pain was rather temporary, the flushing of the extremity continued for a number of hours. The clinical course was generally: (1) immediately after injection—complete relief of pain with rarely three injections necessary; (2) within twenty-four hours—decline of temperature to normal in seventy-two to ninety-six hours; (3) reduction in edema in the first twenty-four to forty-eight hours with complete disappearance of swelling in seven to ten days (average four days).

Sympathetic nerve block, based on sound clinico-pathologic investigation and not empiricism, reduced the duration of illness in acute femoral thrombophlebitis from four weeks with supportive therapy to an average of four days!

Edwards and Hingson, in 1942,[8] developed continuous caudal analgesia in obstetrics, proving that the fractional or continuous principle of anesthesia, first suggested by Lemmon in spinal anesthesia, could be used over many hours for the control of pain. With caudal anesthesia, the sympathetic nerve fibers to the extremity running in the rami communicantes, and traveling with the sensory fibers of nerves are routinely blocked in the epidural space. Continuous caudal anesthesia was next used in the specific treatment of thrombophlebitis of the leg by these same investigators in 1943.[9] Thus, a single needle insertion technique was substituted for multiple insertions and the sympathetic block was continued for hours with, as Lull and Hingson report, "more efficient release of the vasospastic elements and with more prompt improvement in all signs and symptoms of thrombophlebitis."[10]

Continuous Caudal Anesthesia Technique

Hingson, Edwards, and Southworth's technique[8, 11] is the injection of 30 c.c. of (usually) 1.5 per cent metycaine in Ringer's solution into the sacral space through the sacral hiatus. A Hingson malleable 19 gauge 2½-inch or 3-inch needle is preferred. Twenty c.c. of the solution is injected per hour for four hours or more for prolonged effect. This cycle of four-hour treatment may be repeated once or more with interspaced "rest" periods, the needle being left in situ during the entire treatment. During this time, the patient is free to lie on the side or back with the legs elevated to 15°.

Complete relief of pain is reported within fifteen minutes after caudal injection, and no resumption of the discomfort is usually reported by the patient throughout the course of twelve or more hours of treatment. Simultaneous bed rest with slow, regulated exercise is naturally helpful in maintaining muscle tone with the prevention of extension of the thrombophlebitis. The patient is allowed up soon after the course of treatment, the local tenderness having disappeared altogether, with most if not all the edema. An elastic bandage or stocking has been recommended for a week or more, until vascular balance is re-established.[10, 13]

Ellis and Sheffery[12, 13] have added a series of 16 cases of pelvic thrombophlebitis to those (number not revealed) cases of femoral thrombophlebitis recorded by Hingson and Edwards.[9] Also, one case of acute femoroiliac thrombophlebitis, postoperative, cured by continuous caudal anesthesia is reviewed by Urschel and Salley.[14] These four reports are the only articles noted in the literature to date employing the continuous caudal anesthesia technique in such treatment. Not a single case of embolism has been reported following the institution of sympathetic nerve block by either the lumbar paravertebral or the caudal methods.

We have treated five cases of acute postpartum thrombophlebitis of the lower extremity (three deep-femoral and two extensive superficial-saphenous) by continuous caudal anesthesia with spectacular, prompt, and complete cure.

Review of Cases

Table I briefly summarizes the clinical course of these five cases of thrombophlebitis, including the antepartum, intra- and postpartum complications contributing toward septic vascular occlusion.

We, together with others concerned with the problem of postpartum thrombophlebitis, are naturally vitally interested in its prophylaxis. However, it is apparent that neither will transfusions nor sulfa-penicillin therapy insure patients against phlebitis, nor will they cure many patients so affected. However, where these and certain other measures have failed, caudal anesthesia often appears to effect a cure (Cases 1, 3, 5).

Continuous caudal anesthesia was employed in a single course in one instance (Case 3), and in two courses in four patients (Cases 1, 2, 4, 5) in our study of therapy of thrombophlebitis of the lower extremity. Pontocaine and/or metycaine were used as anesthetic agents in all cases. The apparent variation was deliberate in an effort to test these long-acting drugs. However, the standardization of medication, dosage, and duration of treatment of thrombophlebitis by continuous caudal anesthesia are problems requiring further study before the optimum medication and a settled routine of therapy are established.

TABLE I. CASES TREATED

PATIENT	ANTEPARTUM COMPLICATION	LABOR AND DELIVERY	POSTPARTUM COMPLICATION	PRECAUDAL THERAPY	THROMBOPHLEBITIS	CONTINUOUS CAUDAL ANALGESIA
1. L. H. #2316 32 years para i	Antepartum hemorrhage at 30 weeks; partial placenta previa	Spinal anesthesia, shock, version-extraction	Anemia, marked; febrile uterine subinvolution	64 Gm. sulfadiazine, 720,000 U. penicillin transfusions (3)	(Deep) acute right femoral; PP. 29 d.	6 hrs. pontocaine+ 6 hrs. "rest"+ 6 hrs. pontocaine
2. D. H. #6452186 S.M.H. 18 years para i	0	Term; spontaneous	0	0	(Deep) acute right femoral; PP. 7 d.	4 hrs. pontocaine+ 4 hrs. "rest"+ 4 hrs. pontocaine
3. B. J. H. #2581 30 years para iii	0	Term; spontaneous	Breast abscess, left	30 Gm. sulfadiazine	(Deep) acute left-femoral-saphenous; PP. 30 d.	8 hrs. pontocaine
4. M. E. #3265 29 years para iv	0	Term; spontaneous	0	0	(Superficial) acute, segmental (2), right long saphenous; PP. 3 d.	6 hrs. metycaine+ 6 hrs. "rest"+ 6 hrs. pontocaine
5. B. J. #3106 43 years "elderly primipara"	Myomata uteri; typical funnel pelvis; disproportion	Term; elective cesarean section classical	Anemia, moderate; low-grade febrile reaction; uterine subinvolution	400,000 U. penicillin transfusion	(Superficial) acute, almost entire long saphenous; Rt. PP. 13 d.	6 hrs. metycaine+ 6 hrs. "rest"+ 6 hrs. metycaine

One typical case (Case 1) is reported for illustration of the problems involved.

CASE 1.—L. H. No. 1924 and No. 2316. The patient was a 32-year-old, white, unregistered gravida i, with an unmeasured pelvis and a later reported negative Kahn. She was admitted to the Hospital in the thirtieth week of her pregnancy, not in labor, with the history of gross, painless vaginal bleeding. The patient was grouped and cross-matched. Vaginal examination revealed a partial placenta previa, with the cervix 2 cm. dilated but poorly effaced. A cesarean section was advised and she was prepared for surgery. The patient was given 4 c.c. of a 1.5 per cent metycaine in Ringer's solution as an initial dose for continuous spinal anesthesia. The injection was apparently an intravascular one and she sank into profound shock. After about one hour she had revived with plasma, blood, oxygen, and stimulants. The fetal heart remained good throughout and bleeding slackened. Section was abandoned and the membranes were ruptured artificially. Twelve hours later the patient went into spontaneous labor, again with brisk bleeding and recurrent shock. More blood was administered and, at 4 cm. cervical dilatation, a foot was brought down and a relatively easy version effected. The infant, a normal male weighing 5 pounds, was delivered soon after and survived. The mother, still in shock, improved after three transfusions and supportive therapy, but without sulfonamides. She left the hospital on the eleventh postpartum day recovered, though still slightly anemic. No gross lacerations had been sustained at delivery, and the temperature had been elevated (100.4° F.) only on the second postpartum day.

The patient was readmitted to the hospital nineteen days later because of severe, left lower quadrant pain beginning five days before. There was radia-

tion of the pain to the left groin and down the leg. Definite swelling and pain in the left groin had been noted for three days prior to admission. She had been placed on sulfadiazine (1.0 Gm. every 4 hours) two days prior to admission by her local physician. Penicillin was begun upon entry into the hospital (30,000 U. every 3 hours). After six days of sulfonamides and four days of penicillin therapy, the patient was unimproved. The abdominal pain was less, but an acute femoroiliac-femorosaphenous thrombophlebitis had developed. Instead of the temperature falling with chemotherapy, it had risen to 102° F. Edema of the leg and ankle (2+) had developed, and pain and gross nodulation in Scarpa's triangle, with inability of the patient to move the blanched left leg, had resulted. Seven hundred and twenty thousand units of penicillin had been given and chemotherapy was abandoned.

The patient then received continuous caudal anesthesia with 0.15 per cent pontocaine (45 c.c., initial dose). Analgesia to the costal margin was continued for six hours, a "rest" period of six hours was allowed, and another six hours of caudal anesthesia administered with the needle left in the sacral hiatus through the entire eighteen hours of treatment.

A prompt and astonishing improvement resulted. The patient no longer experienced pain in the groin, though tenderness over the femoral vessels remained for twenty-four hours longer. The swelling disappeared, and gradually the temperature fell from 102° F. to normal in twenty-four hours, to remain so thereafter. The white blood count dropped from 14,000 to 6,600, and the sedimentation rate from 31 to 20 mm./hr. (Cutler) in four days. Disability was eliminated, and the patient was active in bed from the day after caudal anesthesia to ambulation two days later. She was discharged seven days after therapy, or twelve days following readmission, and was completely recovered. There were no complications or unpleasant reactions to caudal anesthesia.

Therapeutic Results

Table II is a review of the relief of thrombophlebitis of the lower extremity following continuous caudal anesthesia therapy. Pain was dispelled in all cases immediately after the analgesia "take." Pain did not recur in the "rest" period, or prior to the second course of caudal anesthesia. Objectively, after the institution of caudal, the temperature fell to normal to remain so thereafter in twelve hours in two cases (Cases 2 and 5), and in twenty-four hours in three cases (Cases 1, 3 and 4). Edema (2+) was dispelled in Case 5, after only six hours of caudal analgesia (extensive superficial thrombophlebitis), although in a comparable instance (Case 4) with less edema (1+), thirty-six hours were required for swelling of the leg to disappear. Twenty-four hours after the institution of caudal, there was complete resolution of edema in three cases (Cases 1, 2 and 3) of deep thrombophlebitis. Thrombophlebitis (or other complications) did not recur in any case, and all five patients treated recovered completely—to be ambulatory in forty-eight to seventy-two hours.

Discussion

We have noted that early, acute cases of postpartum thrombophlebitis of the lower extremity are most amenable to continuous caudal anesthesia. If allowed to run a chronic course, it is recognized that thrombophlebitis is followed by a perivascular fibrosis, and resultant edema cannot be easily resolved. Collateral circulation rarely can be established and pain persists as a sequel to the phlebitis.

TABLE II. RESULTS OF CONTINUOUS CAUDAL ANESTHESIA

PATIENT	PAIN RELIEF (MIN.)	NORMAL TEMPERATURE (HR.)	LOSS OF EDEMA (HR.)	LOSS OF TENDERNESS (HR.)	AMBULATION POST-CAUDAL (HR.)	RECURRENT THROMBOPHLEBITIS	OUTCOME
1. L. H.	15	24	(2+) 24	24	72	0	Recovered
2. D. H.	15	12	(2+) 24	24	48	0	Recovered
3. B. J. H.	30	24	(1+) 24	32	48	0	Recovered
4. M. E.	15	24	(1+) 36	36	48	0	Recovered
5. B. J.	15	12	(2+) 6	24	48	0	Recovered

Since the vicious cycle of "pain-vascular spasm-pain" contributes most to the patients' debilitation, reduction in pain is followed by relief of vascular spasm and disappearance of edema. Pain, moreover, can be controlled completely, promptly, and for a prolonged period by the single caudal needle insertion.

We believe pontocaine and metycaine are nontoxic in the doses recommended and with the usual precautions. It is felt that the prolonged action of pontocaine is often desirable, since frequent injections are obviated. The level to which pontocaine may extend in the epidural space, however, is difficult to predict, and overdosage may occur unless the anesthetist is cautious. In our experience, metycaine is easier to control and the action is moderately prolonged. Furthermore, metycaine can be used for the skin anesthesia as well as for the test dose. We have not used procaine often, even though it is slightly less toxic, because of its brief anesthetic action.

We believe that a level of analgesia to L.1 is sufficient for the treatment of thrombophlebitis of the lower extremity by continuous caudal anesthesia. Using pontocaine 0.15 per cent or metycaine 1.5 per cent solution, approximately 30 c.c. (total initial dose, including an 8 to 10 c.c. test administration) with 20 to 25 c.c. as often thereafter as necessary (one to three hours) is sufficient to maintain analgesia at therapeutic levels. One or two cycles of treatment with the needle left in situ are recommended.

Anemia, hypotension, febrile state, and sensitivity to the anesthetic agent are all factors contributing to unpleasant side effects and possible shock. In our experience, nausea, vomiting, and shock did not occur. Barbital analgesia, together with epinephrine, added ease and safety to the procedure.

The relaxation we have achieved, the relief of pain, and the continuation of effective therapy are not possible save by sympathetic nerve block, and are most profound with continuous caudal anesthesia, in the treatment of acute postpartum thrombophlebitis of the lower extremity. Hingson has indicated that in the metabolism of metycaine, a demerol-like, piperidine ring, may be the partial explanation for the added analgesia and slight euphoria noted with metycaine.[15]

In acute, fulminating cases of thrombophlebitis of the ilio-femoro-saphenous system, continuous caudal anesthesia should be considered the best method of therapy, and chemotherapy should be considered an adjunct.

Summary

1. The development and rationale of sympathetic nerve block by paravertebral and continuous caudal anesthesia in the treatment of thrombophlebitis of the extremity are reviewed.

2. Five cases of acute, postpartum thrombophlebitis of the lower extremity successfully treated by continuous caudal anesthesia are presented.

3. Continuous caudal anesthesia is a sound, simple, superior method of treatment in cases of acute thrombophlebitis of the lower extremity.

The opinions expressed here are those of the author and do not necessarily reflect those of the Navy Department.

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FURTHER OBSERVATIONS ON CAPILLARY FILTRATION RATES IN PREGNANCY*

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A PREVIOUS report[1] indicated that the filtration of fluid through the capillary wall proceeds in the latter weeks of pregnancy at a rate which is somewhat increased over the normal (nonpregnant). Women with toxemia of pregnancy did not exhibit this increase in rate of filtration, presumably because of considerable amounts of fluid already present in the tissues. Since publication of the first report in 1943, twenty-four additional subjects have been studied by the plethysmographic technique previously employed.[1-5] Eight of these were normal controls, eleven were normally pregnant near term, and five were pregnant with signs and symptoms of pre-eclampsia. The filtration rates in these new subjects have been combined with those previously reported, and statistics have been recalculated from the larger samples. While a few further observations were made on postpartum patients, these are not reported here because they add nothing of consequence to the figures already presented.

Observations

1. *Normal, nonpregnant controls.*—In 20 normal women, ranging in age from 22 to 35 years, the mean rate of filtration of fluid from the minute vessels into the tissues of the forearm was 0.109 ± 0.004 c.c. per minute per 100 c.c. of forearm. The range of individual values was from 0.088 to 0.167 c.c. per minute per 100 c.c. of tissue and the eight new observations all fell within the range obtained for the twelve original subjects (Fig. 1).

2. *Normally pregnant subjects.*—In 23 women (11 new observations) observed during the final eight weeks of normal pregnancies the mean rate of filtration was 0.146 ± 0.008 c.c. per minute per 100 c.c. of tissue and the range was from 0.079 to 0.230 c.c. (Fig. 1). Although it is obvious from inspection of Fig. 1 that many individual values for the pregnant subjects fall within the range of control values, yet there is a statistically significant difference between the mean values of the two groups (Table I).

3. *Toxemic subjects.*—In 17 pregnant women (5 new observations) with either pre-eclampsia or arteriolosclerotic toxemia observed late in the last trimester the mean rate of filtration was 0.115 ± 0.009 c.c. per minute per 100 c.c. of forearm, and the range was from 0.048 to 0.177 c.c. (Fig. 1). The average value was not significantly different from that of the controls, but it was *significantly lower* than that of the normally pregnant women. It should be noted that the two lowest individual rates of filtration were found in this group of toxemia patients.

Discussion

The additional observations reported here do not alter in any way but merely substantiate the conclusions reached in the previous report.[1] The figures

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TABLE I. SIGNIFICANCE OF DIFFERENCES BETWEEN MEAN FILTRATION RATES FOR CONTROL, NORMALLY PREGNANT, AND TOXEMIA SUBJECTS

GROUPS	DIFFERENCE BETWEEN MEANS	STANDARD ERROR OF DIFFERENCE	(K)*	P*	SIGNIFICANT DIFFERENCE
Control vs. normal pregnancy	0.037	0.009	4.15	0.0001	Yes
Controls vs. toxemic pregnancy	0.006	0.010	0.60	0.5485	No
Normal pregnancy vs. toxemic pregnancy	0.031	0.012	2.58	0.0099	Yes

Rates of filtration in c.c. per minute per 100 c.c. of forearm.

*(k) is ratio of difference to its standard error. P is probability of the (k) magnitude being exceeded solely through errors of random sampling.

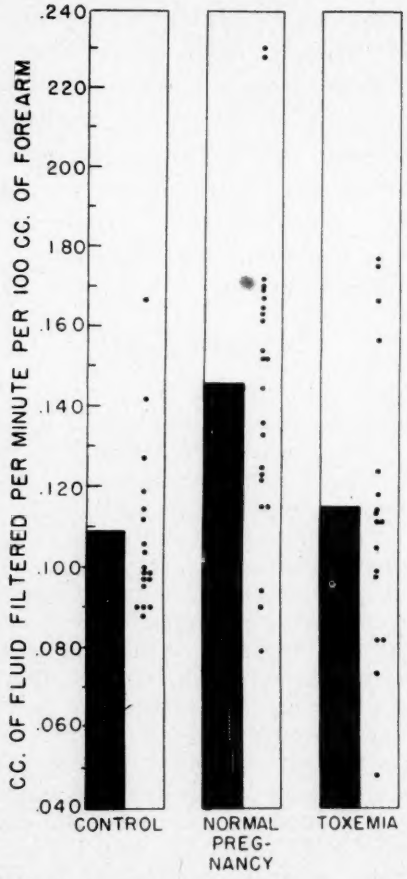

Fig. 1.— Rates of filtration in control subjects, normal pregnant women, and pregnant women with toxemia. The top of each solid column indicates the respective mean value.

still seem to indicate that, for the group as a whole, normally pregnant women permit the filtration of fluid from minute blood vessels into forearm tissues at a more rapid rate than do nonpregnant women or pregnant women with some form of toxemia of pregnancy. The precise mechanism of this phenomenon, granting the validity of the conclusion, cannot be satisfactorily explained on the basis of present knowledge, and nothing of importance can now be added

to the discussion presented in 1943. The obvious inference is that the permeability of the capillary wall is for some reason increased in the pregnant woman, at least in the face of intracapillary pressures which are above the normal range. However, despite the comparative ease with which fluid leaves the vessels in the pregnant patient, some mechanism seems to be operating to retain fluid within the vascular system under normal circumstances. If this were not so, one would expect to find generalized edema much more commonly in association with normal pregnancy. With respect to the mean filtration rate in the toxemic group and the very low individual values observed in these subjects, it might simply be pointed out again that filtration is diminished in the presence of elevated tissue pressures built up by pre-existing edema fluid. One would predict, then, a comparatively low rate of filtration for the toxemic patient with an already established generalized edema. In other words, the plethysmographic technique used in this study is not helpful in determining whether the capillaries of toxemic patients are more permeable than usual, as might be postulated, since filtration has preceded the experimental observations and the *rate* of further transfer of fluid is necessarily diminished. For a complete discussion of the relation of tissue pressure to filtration rate, the reader is referred to the fundamental paper by Landis and Gibbon.[3]

Summary and Conclusions

Twenty-four additional observations on the rate of filtration of fluid through the capillary wall, obtained with a pressure plethysmograph, have been combined with figures previously reported and new statistics have been computed. The more recent values tend to corroborate the previous conclusion that the rate of filtration through the capillary wall is somewhat increased over the normal in the last eight weeks of normal pregnancy. No satisfactory explanation for this finding is presently available. Patients with toxemia of pregnancy do not exhibit this increase in rate of filtration, presumably owing to the fact that they have sufficient edema to interfere to some extent with further filtration of fluid into the tissues.

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CYSTIC ADENOMYOSIS OF THE UTERUS

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ADENOMYOSIS of the uterus is a well-recognized cause of pathologic hemorrhage and dysmenorrhea; the cardinal symptom, namely, menorrhagia or metrorrhagia, may occur without any complicating abnormality. Hemorrhage is explained by the endocrine dysfunction that exists. The endocrine dysfunction is manifested by a well-marked hyperplasia of the endometrium. Dysmenorrhea is explained by the invasion of the islands of endometrium which may cause painful contractions of the uterine musculature.

Adenomyosis is defined as the heterotopic occurrence of islands of endometrium into the uterine wall. It is a benign invasion of the endometrium into the uterine musculature, and is associated with a diffuse overgrowth of the musculature.

Incidence

There is a great variability in the reports of the incidence of adenomyosis. Fallas and Rosenbloom[1] reported an incidence of 49.6 per cent in 260 cases of endometriosis. Counsellor,[2] in 884 cases of endometriosis, found an incidence of 69.6 per cent. Lewinski[3] reported that 53.5 per cent of all uteri removed at necropsy showed adenomyosis, and therefore called the findings mainly physiologic. Frankl[4, 5] disagreed with this high incidence. Over a ten-year period at the Alexander Blain Hospital[6] there were 73 cases of adenomyosis, representing an incidence of 10.7 per cent of all uteri removed. At the Royal Victoria Montreal Maternity Hospital, in 1944, there were 60 cases of adenomyosis in 236 uteri removed for various reasons, representing an incidence of 25 per cent of all uteri removed.

The age incidence varies from 25 to 50 years. It is usually found within the active sex life of an individual, but may be found in women past the menopause. Frank and Geist[7] studied a series of 203 cases of adenomyosis. In this group 23, or 11.3 per cent, were women past the menopause. Dreyfuss[8] reported an average age of 46 years for adenomyosis. Shamnakis[9] found that 90.6 per cent were between 30 and 60 years, and 53.6 per cent were in the fifth decade. Adenomyosis is a disease of the second half of the generative period, and there is usually a history of many pregnancies.

Histogenesis

The pathologic diagnosis of adenomyosis rests on the demonstration of epithelial and stromal elements closely resembling the endometrium within the uterine musculature. Numerous theories have been postulated to explain the origin, and it would appear from a review of these theories that no single mechanism is universal in the pathogenesis of the disease.

Theories

1. Cullen,[10] and Frankl[4, 5] postulated a theory of direct invasion of the uterus by normal endometrium. The stroma of ectopic islands derived from the mucous membrane prepares the way for glands to follow. In this connection it is interesting to note that, in 1923, Robert Meyer[11] showed that the stroma of endometrial islets destroys the myometrium. Destruction is not

restricted to the interstitial tissue but involves the muscle cells, i.e., the myofibrils which are responsible for the function of muscle. The most aggressive types of adenomyosis are those with a very cellular stroma. Frankl has shown that there exists a continuation of the mucous membrane beyond its normal border line. Adenomyosis is not related to any inflammation.

2. Cullen:[10] The islands of ectopic endometrium represent misplaced remnants of the Müllerian duct epithelium.

3. von Recklinghausen[12] and Pfannenstiel:[13] The epithelium originates from the mesonephric tissue of the Wolffian duct.

4. Iwanoff[12] and Novak:[14] Adenomyosis arises from the activation of celomic rests.

5. Meyer:[15, 16] Adenomyosis arises from epithelial heterotrophy dependent on an inflammatory or hormonal stimulus.

6. Adenomyosis is a result of fetal budding of the epithelium, or represents misplaced islands of fetal mucosa.

7. Halban,[17] Bertner,[18] and Sampson:[19-22] Adenomyosis is a result of lymphatic or hematogenous spread of endometrium, i.e., metastatic deportation of glands. Fragments of endometrial tissue may be disseminated into the venous circulation during menstruation from the mucous membrane lining the uterus. This endometrial tissue, set free by menstruation, may continue to grow if transported to a favorable environment.

8. Brines and Blain[6] suggested that adenomyosis was a result of spontaneous generation of endometrial stromal or interstitial cells from and within the myometrium. They advanced the theory that by a process of dedifferentiation or metaplasia, cells less mature but highly specialized were produced. These cells possessed the potentiality to differentiate into epithelial cells, which formed endometrial glands. The process was comparable to the differentiation of fibroblasts into osteoblasts and chondroblasts. The stromal cells were formed before the glands. This was borne out by the fact that small islands of stromal cells were encountered which, by serial section, were found to be unassociated with gland formation.

Pathology of Adenomyosis

The gross characteristics of adenomyosis reveal a slightly or markedly enlarged uterus due to a diffuse overgrowth of the musculature that is part of the lesion of adenomyosis. The enlargement is usually diffuse and symmetrical, but asymmetrical enlargement may be a feature when there is irregular distribution of the islands of endometrium. On section the gross surface reveals a trabeculated appearance, but there are no circumscribed nodules as seen in myomas. There are indefinite nonencapsulated areas of hypertrophied smooth muscle bundles. There are dark hemorrhagic or chocolate-colored areas which vary from a few millimeters in diameter to large cystic spaces several centimeters in diameter. Large cysts, however, are rare. The microscopic cysts and islands of tissue are scattered discretely through the musculature. Adenomyosis ranges from minute incursions of endometrium to extensive foci far removed from the endometrium. In the majority of cases the ectopic endometrium is situated in the inner half of the uterine wall and often communicates with the mucosal layer.

The pathologic diagnosis is based on the microscopic findings of endometrial islands of glands and stroma within the uterine muscle. The ectopic foci show the typical histologic gland and stroma structure. There are wide variations in regards to the functional state of the endometrium. Complete cyclical changes may be revealed, but usually the ectopic areas respond only to estrogenic stimulus. Thus the aberrant tissue seldom shows secretory activity. Actual bleeding into the glands seldom occurs. In many cases there is an associated endometrial hyperplasia.

Case Reports

Two cases of cystic adenomyosis from the gynecologic department of the Royal Victoria Montreal Maternity Hospital are presented. These are outstanding because of the large size of the cysts.

CASE 1.—A para 0, aged 36 years, who was admitted with complaints of dysmenorrhea which had become severe for the last six months; and menorrhagia of six months' duration. Family history and personal history were noncontributory, except that she had a complete abortion at two months in 1939. The dysmenorrhea was premenstrual in time. The menstrual periods started at 14 years of age, were regular every 26 to 28 days, and lasted 2 to 3 days. The menorrhagia was manifested by profuse flow which was prolonged to five days for the last six months. Physical examination revealed a normal, healthy, and well-developed woman. Pelvic examination showed a nulliparous, healthy vulva and vagina. The cervix was edematous, the external os circular and healthy. The uterus was anteverted, anteflexed, mobile, and irregularly enlarged to the size of a three months' pregnancy. The appendages were normal on palpation.

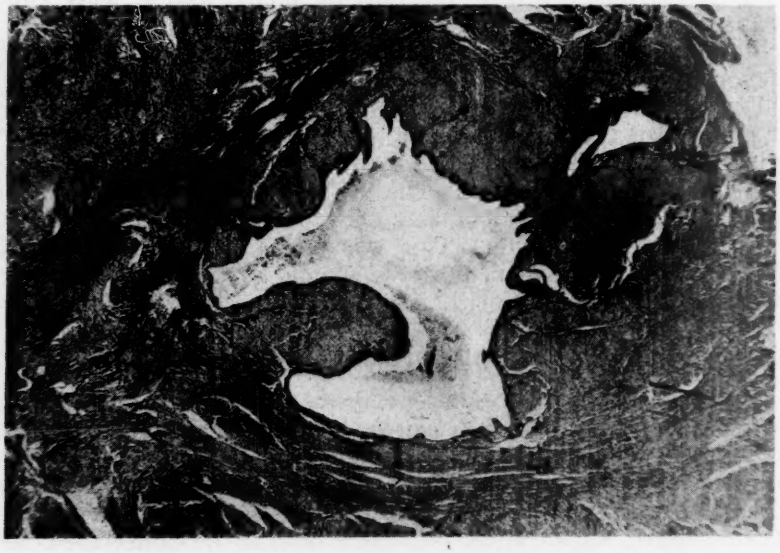

Fig. 1.—Cystic adenomyosis, low power (×20).

On June 16, 1945, a supravaginal hysterectomy, bilateral salpingo-oophorectomy, and appendectomy were performed. The uterus was grossly irregular and measured 15 by 9 by 7 cm., the seat of intramural fibromyomas. Both ovaries were slightly enlarged and cystic. The pathologic examination revealed a large cystic space in the myometrium (Fig. 1) which was lined by typical endometrial cells of low columnar variety. The rest of the microscopic examination revealed a premenstrual endometrium, fibromyomas uteri, and follicle cysts of the ovaries.

CASE 2.—A para iv, aged 32 years, who was admitted with complaints of menorrhagia and dysmenorrhea for six years. Before her last pregnancy in 1939 her periods were regular and normal, lasting five days. Menarche started at 12 years of age. Gradually, since 1939, menorrhagia had become marked, and the flow lasted between fourteen to twenty-one days each month. Dysmenorrhea with radiation of pain to the lumbosacral region had become severe.

Her last period lasted five weeks. Family history and personal history were noncontributory. Physical examination revealed a thin, pale, white female. Blood determination on May 17, 1945, showed a hemoglobin of 54 per cent, white blood count of 10,500, and a sedimentation rate of 38 (23 conjugata vera) mm. Fasting and postprandial sugars were 96, and 119 mg. per cent, respectively. Pelvic examination revealed a normal parous vulva and vagina, and a firm, healthy cervix. The uterus was anteverted, anteflexed, and en-

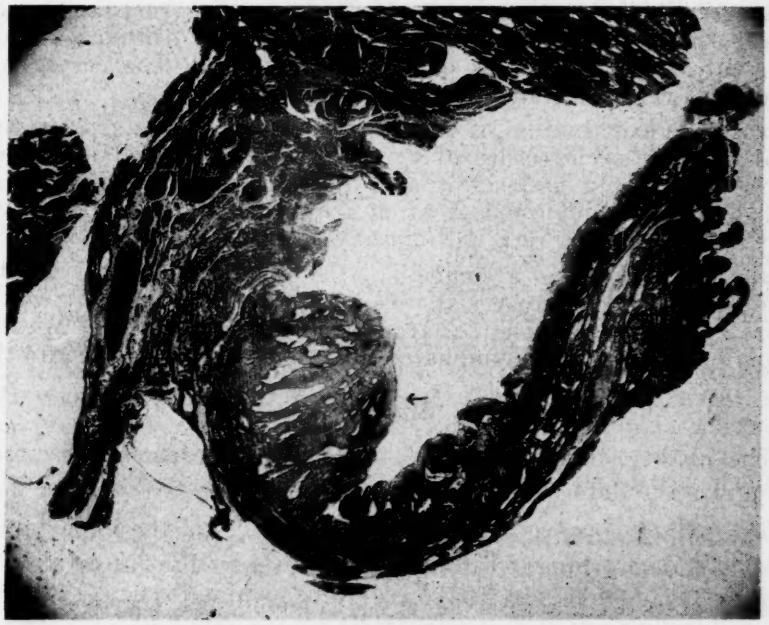

Fig. 2.—Cystic adenomyosis, low power (×20).

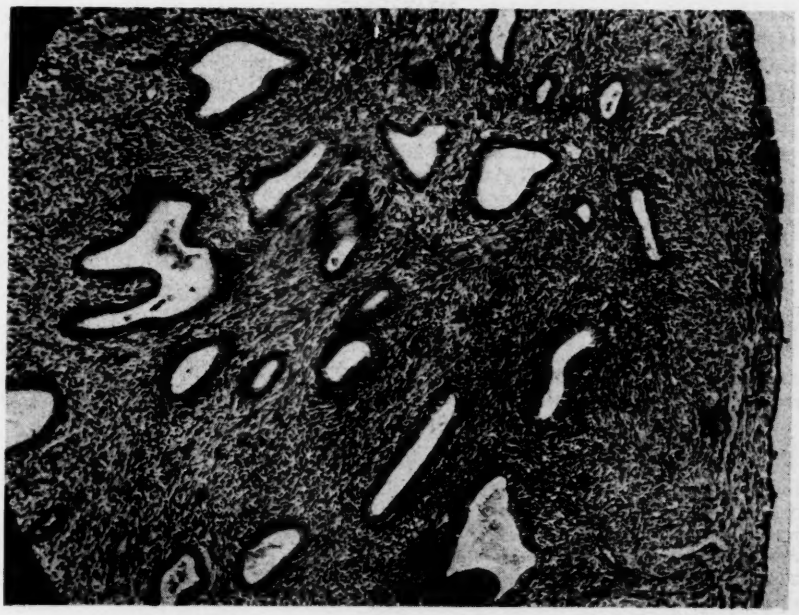

Fig. 3.—Cystic adenomyosis, high power of Fig. 2 (×400).

larged to the size of a seven weeks' pregnancy. The appendages were clear. On May 19, 1945, a 600 c.c. blood transfusion was given. On May 21, 1945, the hemoglobin was 63 per cent; red blood cells, 3,500,000; platelets, 210,000; prothrombin time, 45 seconds; fibrin time, 2 minutes, 10 seconds; complete coagulation, 11.5 minutes.

On May 28, 1945, total hysterectomy was performed. The Fallopian tubes and ovaries were healthy and were not removed. The uterus measured 15 by 10 by 8 cm. On section, in the region of the fundus, an intramural cyst 3.5 cm. in diameter and filled with sanguinous fluid was discovered. This cyst communicated with a smaller cyst 1.5 cm. in diameter. Circumscribed nodules were present throughout parts of the uterine wall. The cervix on section showed dilated cervical glands.

Microscopic examination of the cysts described in the gross revealed that they had a lining architecture of typical endometrium, glands, and stroma. These are represented under low and high magnification in Figs. 2 and 3. The rest of the pathologic examination showed cystic cervicitis, polypoid hyperplasia of the endometrium, and fibromyomata uteri.

While adenomyosis is a common pathologic entity today, the finding of macroscopic cystic adenomyosis is rare and worthy of note. It would appear that these cysts could arise either from misplaced remnants of Müllerian duct epithelium or as a result of lymphatic or hematogenous spread into the uterus.

Summary

1. The history, incidence, and histogenesis of adenomyosis are reviewed and brought up to date.

2. The pathology of adenomyosis is described and the important features, viz., ectopic endometrium and diffuse overgrowth of the musculature, stressed.

3. Two cases of macroscopic cystic adenomyosis are described and the microscopic pathology is presented.

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SOLID TERATOMAS OF THE OVARY WITH NEUROLOGICAL METASTASES

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(From the laboratory of St. Thomas Hospital)

IF MALIGNANT changes occur in solid teratomas of the ovary, they are seen almost exclusively in elements of the nervous tissue, and in those of the digestive or of the respiratory tract.[1, 2, and others] Peritoneal implantations of nervous tissue derived from an ovarian teratoma, however, are apparently rarities. Only ten such cases have been reported.[3-10] It was, therefore, deemed worth while to present one more case, and to compare the histologic characteristics and clinical behavior of the group.

Case Report

A 22-year-old woman complained of abdominal pains and swelling of the abdomen for four months. Physical examination revealed a soft, cystic tumor filling the entire pelvis and extending from the right lower quadrant toward the left upper quadrant. The uterus was not palpable. Abundant colostrum was present in both breasts. The Aschheim-Zondek reaction was negative. Upon laparotomy there was found considerable ascites. The greater omentum was covered with numerous whitish, opaque nodules approximately 2 mm. in diameter; it was attached to a tumor of the *right* ovary. This tumor was of elastic consistency extending upward to the spleen. After its removal another tumor of the *left* ovary was found and extirpated. The latter was somewhat larger than a man's fist. Its surface was smooth and whitish-yellow in color. A piece of omentum was removed for histologic examination. After having x-ray treatment the patient was observed and in good condition for fifteen months postoperatively.

The tumor of the right ovary measured 22 by 19 by 10 cm. after being fixed in 10 per cent formol. It weighed 1,750 Gm. and was completely surrounded by a grayish fibrous capsule. In general, the tumor was nodular and firm in consistency; some of the nodules were gray, others were yellowish-gray. In one area was a tense translucent cyst. The cut surface was gray, and numerous fibrous septa divided the tumor into nodular masses of varying size. Scattered throughout the tumor were numerous cysts measuring as much as 1 cm. in diameter. Some of them contained clear gelatinous fluid. The Fallopian tube of this side could not be found.

A nodule composed of fat tissue and covered by skin and hair had been enucleated during the operation. It was about 2 cm. in diameter.

The piece of omentum was infiltrated by abundant whitish, faintly lustrous nodules, measuring 2 mm. in diameter.

The tumor of the left ovary was ovoid in shape, measuring 10 by 7 by 6 cm. It was composed of two communicating cysts. Attached to it was the unaltered Fallopian tube. One of the cysts was empty, the other contained sebaceous material and light brown hair. After the removal of the sebaceous material a plug the size of a hazelnut became visible in which bone particles could be palpated.

Histologic examination.—Tumor of the right ovary: About $\frac{1}{6}$ of the tumor consisted of fat tissue, the other $\frac{5}{6}$ was mainly composed of nervous tissue. There were also irregularly shaped small and minute islands of hyaline cartilage, rather cellular, and surrounded by a capsule of fibrous tissue. Next to these islands were mucous glands, arranged either singly or in small groups. There were small pieces of lamellar bone with fibrous bone marrow and nearby cysts of varying structure and size, mostly round, sometimes irregularly shaped, situated partially within the nervous tissue. Adjacent to some of these cysts were a few sebaceous glands and single hairs.

The greater part of the tumor was composed of neuroglia. The glia cells had scant cytoplasm, the processes often were numerous and short. In some areas the glia cells were more compactly arranged. The areas composed of nervous tissue were usually surrounded by fibrous tissue, rather poor in nuclei and blood vessels, and having in some regions a gyrus-like structure (Fig. 1). There were, however, neither typical layers of ganglion cells nor "subcortical" formations of white substance. In other parts were ganglion cells of different shapes and everywhere appearing fully mature. They had the typical large nucleus with nucleolus and axones as well as dendrites in varying numbers (Fig. 2). Sometimes they were also apolar, pyramidal, or round. Myelin sheaths were nowhere to be found.

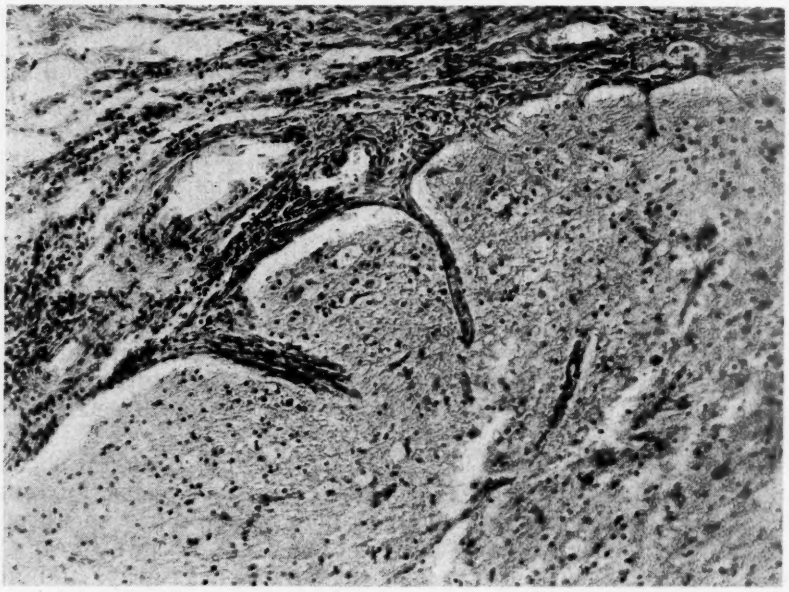

Fig. 1.—"Gyrus"-formations of the nervous tissue (large tumor of the right ovary) (×172).

Considering the irregularity of the nervous tissue, it was surprising to find a completely developed cerebellar cortex in the upper pole of the tumor. There was, corresponding to the normal, an internal granular layer, a single layer of Purkinje cells, and an external gray substance with capillaries arising from the leptomeninges (Fig. 3).

Occasionally there appeared a few sympathetic ganglia. Bundles of normal-appearing nerve fibers occupied larger areas of the tumor. Less numerous were proliferations of the neuroepithelium, irregularly shaped tubules lined by high cylindrical epithelium. As often described in teratomas there were numerous chorioid plexuses to be seen.

The small, enucleated tumor contained fat tissue that was covered by skin and its appendages. In addition, there were a few smaller cysts lined by melanin-containing cells, one small island of cartilage, and a few small bundles of smooth muscle fibers.

The piece of omentum contained well-circumscribed ovoid and irregularly shaped nodules of neuroglia. The latter was rather poor in cells and located among the fat tissue of the omentum. In some regions these nodules were very numerous, so that almost no fat tissue was to be seen. Ganglion cells and neuro-epithelium were absent. Here and there a few groups of small round cells were present. In some areas they appeared more densely arranged and here their shapes were somewhat irregular.

Sections through the plug of the dermoid cyst of the left ovary showed cornifying stratified squamous epithelium, sebaceous glands, sweat glands, with dilated lumina, hair follicles, bundles of smooth muscle fibers, and cartilage. In addition, there were a few islands of neuroglia, small nerve fibers, and one sympathetic ganglion.

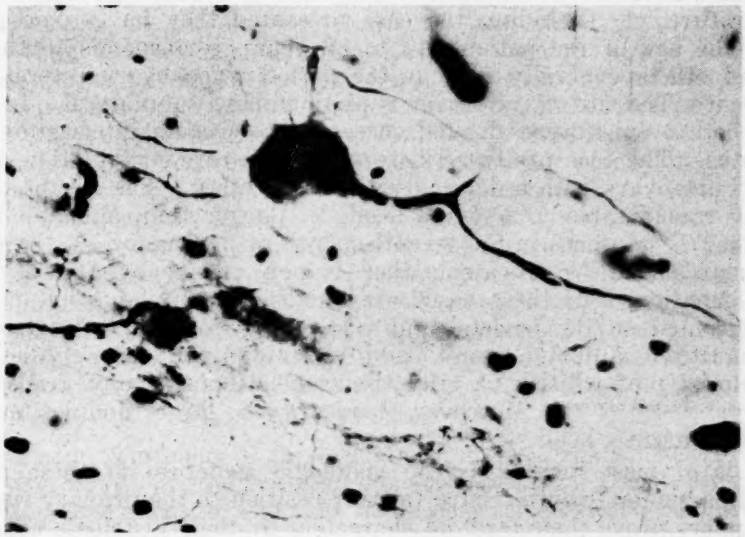

Fig. 2.—Multipolar ganglion cell (large tumor of the right ovary) (×662).

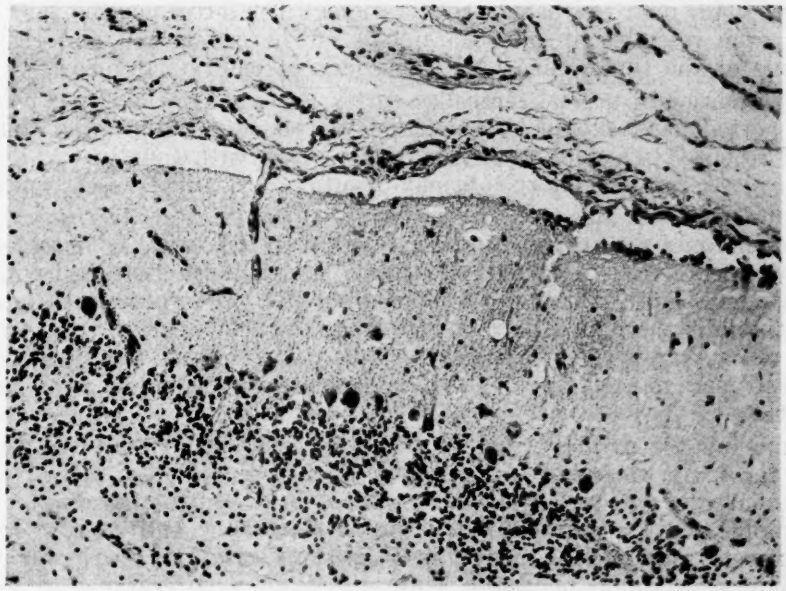

Fig. 3.—Cerebellar cortex (upper pole of the large tumor of the right ovary) (×172).

Discussion

The above-described case offered a few peculiarities. There was a combination of a simple dermoid cyst (cystic teratoma) of one side with a solid teratoma of the other ovary that gave rise to metastases. Furthermore, the small amount of neuroepithelial tissue within the giant complex of nervous tissue was remark-

able. Rarely, one of the numerous sections showed the well-known pictures of the neuroepithelial tubules with their high cylindrical lining. Embryonal neuroglia was entirely absent. There were also histologic gyrus-like formations of the nervous tissue, and in the upper pole of the tumor a perfectly developed cerebellar cortex with leptomeninges.

There are 10 cases of neuroglial metastasizing ovarian teratomas reported in the literature.[3-10] Including the case presented they have some points in common. The age of the patient, 11 to 38 years, corresponds to that which Miller[11] and others generally give as the period when ovarian teratomas are most frequent. The site of the tumor is predominantly unilateral. In one case (v.Bary[8]) both ovaries were affected successively with an intervening interval of six months. The case presented here shows the rare combination of a solid teratoma of one ovary with a dermoid cyst of the other. The size of the tumor is generally considerable ("a man's head,"[5] "larger than a man's head,"[3, 4] "watermelon,"[7] "a uterus in the seventh month of pregnancy,"[8] "half as large again as a man's head"[7]). As a rule, there is more or less abundant ascites. The metastases mentioned in these cases are exclusively implantation metastases. They are situated on the parietal and visceral peritoneum and omentum and appear as multiple, miliary ("small" and "minute") nodules or "vesicles" ("as in tuberculosis") of whitish or gray tissue, gelatinous, glassy, translucent, or opaque.[3, 4, 5, 6, 10, and our case] Moreover, there are also larger nodules, even up to the size of an infant's head.[7, 9]

What is of most interest is the histologic structure of these peritoneal metastases, particularly with regard to their relation to the primary tumor. All primary tumors prove their teratoid characters by their histologic composition; yet the predominance of the elements of the nervous tissue indicates their ability to proliferate. There are almost everywhere fully mature elements of the nervous tissue, except for neuroepithelial proliferations. The latter may be very marked and may even resemble an adenocarcinoma.[7] The ectodermal and entodermal components of the tumors show the same lack of embryonal forms.

The formation of typical cerebellar cortex, as found in the upper pole of the tumor reported here, should be particularly stressed. Willis[12] and Bettinger[13] described recently two solid teratomas of the ovary with equally well-developed cerebellar cortices. Askanazy[14] briefly mentioned a third case, but gave no detailed description.

At other times the nervous tissue may occur in the form of microscopic gyri (Buettner[5] and the case reported) or it may be highly differentiated with layers of ganglion cells and remnants of leptomeninges.[7, 8] Most prominent among the nervous tissue is the neuroglia. It is fully mature in nearly every case. Exceptions are v.Bary's[8] and Schairer's[9] cases. The former mentions neuroglia of "marked malignant character," the latter describes "immature" elements of nervous tissue.

Comparing the primary tumors with the peritoneal metastases, the latter were by far more uniformly constructed. They were almost exclusively composed of neuroglia and were well differentiated in five of the ten cases. Fleischmann[3] emphasized its embryonal structure, Neuhaeuser[4] and v.Bary[8] report its resemblance to round-cell sarcoma; in Ruzicska's case III[7] there was found a combination of cellular neuroglia with glandlike proliferations of epithelial tubules, and Schairer[9] describes cartilage and bone intermingled with mature and immature neuroglia.

The question arises, does the histologic structure of the primary tumor or of the metastases determine the clinical course? Of the eleven cases, the patient's fate is "unknown" in two.[7] Consequently, there are nine cases remaining to answer the above question. In five cases, including the case presented, the

period of observation extended two years—a comparatively short period. The other four cases ended in death (Fleischmann,[3] Schairer,[9] Ruzicska,[7] v.Bary:[8] four and twenty-four months after the first symptoms, seven and nine months after operation, respectively). In these four cases, some metastatic nodules had to be left on the peritoneum. This, however, is unimportant, for there was abundant tumor tissue left in five cases[4, 5, 6, 10, our case] that remained free from any recurrence of the tumor. Apparently the metastatic nodules may undergo regressive changes after removal of the primary tumor.

In the four fatal cases, the histologic descriptions of the tumors indicated definite derivatives from normal tissue. Fleischmann[3] characterized the neuroglia as "embryonal," Ruzicska[7] described in his second case the proliferations of the ependyma as "resembling an adenocarcinoma," v.Bary[8] recorded a "glioblastic sarcoma," and Schairer[9] "immature" neuroglia at autopsy. Consequently, it would appear that any marked cellularity of the nervous tissue in the primary tumor or in the metastases would indicate an unfavorable clinical course. The "glioblastic sarcoma" represents a special form of malignant change occurring in the teratoma of the ovary. It may, however, be stated that the clinical behavior of ovarian teratomas with neuroglial metastases on the peritoneum corresponds to the doubtful clinical course of solid teratomas in general.

Summary

To ten solid teratomas of the ovary with neuroglial metastases on the peritoneum reported up to the present, one has been added that contained fully developed cerebellar cortex and that was associated with a dermoid cyst of the other ovary. The neuroglial metastases from solid teratomas of the ovary are dissemination metastases on the peritoneum. They consist almost always of pure neuroglial tissue. In exceptional cases there may be proliferating neuroepithelium, cartilage, or bone among the neuroglia. The nervous tissue of the primary tumor may be highly developed (ganglion cells of various mature types; ganglion cells arranged in layers with remnants of meninges; gyrus formations; cerebellar cortex). The neuroglia in both primary tumor and the metastases may be fully mature, of an "embryonal" type, resembling a round-cell sarcoma, or of marked malignant character similar to a glioblastic sarcoma. According to the clinical observations, the neuroglial metastases of mature tissue seem to degenerate and disappear after extirpation of the primary tumor. Extremely cellular or immature neuroglia in the primary tumor or in the metastases may give rise to recurrences, and finally cause death.

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BILATERAL SIMULTANEOUS TUBAL PREGNANCY

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THE infrequency with which one comes in contact with bilateral tubal pregnancy in the literature for the past ten years impresses upon one the rarity of this condition. When an authentic case is encountered in an Army General Hospital which has only a small Women's Surgical Section, it is likely to attract more than the usual amount of attention.

This patient, Mrs. Mabel P., aged 21 years, the wife of an Army sergeant, was brought to the Oliver General Hospital in an automobile by her husband at about 10:30 P.M., on March 6, 1946. She stated that she was at a dance, and after dancing about ten minutes she experienced a severe pain in her left lower quadrant. This pain very quickly became generalized throughout her abdomen. She became nauseated, vomited, and subsequently fainted. After she had been revived, she noted a small amount of vaginal bleeding. She was brought to the hospital immediately.

On admission, her pulse rate was 80, respiration 15, and temperature 97.8° F. She was seen by the Surgical Officer of the Day who believed she had a threatened abortion. Morphine, an ice cap to the abdomen, and the Trendelenburg position were ordered.

She was seen by the gynecologist on the morning after admission. Pain in both shoulders, generalized abdominal pain, faintness, and weakness were her chief complaints at this time. She stated that her last menstrual period had been January 15, 1946. Previous to this time she had always been regular. In the past two or three weeks she had experienced some enlargement and soreness of her breasts. Also, she had morning nausea on several occasions. She had had one previous pregnancy which terminated two one-half years ago with a normal delivery. A moderately severe toxemia accompanied this pregnancy. She gave no history of any abortions or miscarriages.

The physical examination revealed a well-developed woman who was very pale, had an anxious look on her face, and appeared acutely ill. The skin was moist and clammy. The conjunctiva and buccal mucous membranes were very pale. The breasts were moderately firm, with Montgomery glands present. There was an increase in the secondary areolar tissue. Her pulse was regular, thready, and the rate was 152. The blood pressure was 80/42. While making preparations to administer intravenous fluids, the systolic pressure dropped to 60. There were no murmurs, thrills, or enlargement of the heart. The lungs were clear.

The abdomen was moderately distended, and there was extreme tenderness throughout, most marked in the lower quadrants. No masses could be felt. A definite fluid wave was present. There was shifting dullness to percussion and moderate muscular rigidity throughout the abdomen, as well as rebound tenderness. Loud peristalic sounds were heard in all areas.

The pelvic examination revealed a firm perineum. The cervix was exquisitely tender to manipulation, and slightly softened. Visualization showed some bluish discoloration. Due to the patient's extreme tenderness, the uterus and adnexae could not be satisfactorily outlined. However, after she had been anesthetized for operation, a thickening of the uterine end of the right tube and a fullness in the left adnexa could be felt. However, no discrete masses could be demonstrated.

Immediately following the examination, 1,000 c.c. of 10 per cent glucose in normal saline was given intravenously. This was followed by 500 c.c. of whole blood. The blood pressure responded rapidly to this treatment.

An uncatheterized urine specimen, which had been taken earlier in the morning, showed a 4 plus albumin. The microscopic examination revealed many epithelial cells, granular casts, and a few white blood cells. Essentially the same report was later received on a catheterized specimen. A white blood count done at the time of the first urinalysis showed 44,950 leucocytes. The complete blood count report received later showed a 70 per cent hemoglobin, 3,330,000 red blood cells, and 43,700 white blood cells with the following differential count; neutrophiles 83 per cent, lymphocytes 16 per cent, and monocytes 1 per cent. The N.P.N. at this time was 31.5 milligrams.

After the administration of intravenous glucose and blood, the patient's blood pressure reached 100/62, and the pulse rate was approximately 112 per minute. It was then thought that the patient was sufficiently out of shock to tolerate an anesthetic and laparotomy.

Operation.—The vagina was prepared, and a 17 gauge needle was inserted in the cul-de-sac. Some old, free blood was obtained. The abdomen was then opened in the midline. Before opening the peritoneum, it was noted that this tissue had a typical bluish color. When the peritoneal cavity was entered, a large amount of old, free blood, and many large clots were found. About 1,500 c.c. of blood and the clots were removed. A ruptured ectopic pregnancy, bleeding freely, about one one-half inches long and one inch in diameter was found in the middle third of the left tube. An unruptured ectopic pregnancy of approximately the same size was found at the uterine end of the right tube. Both tubes, including the pregnancies, were excised. The peritoneum was closed with plain catgut and the fascia with doubled No. 1 chromic catgut. The skin was closed with three silkworm gut tension sutures and silk. On several occasions during the operation the patient had a fall in blood pressure and a rise in pulse rate. In order that the operation could be completed as quickly as possible, no additional exploring was done.

While on the operating table, an additional 500 c.c. of whole, fresh blood was started. This was given slowly and was completely administered about

two one-half hours after the patient returned to bed. When she returned from surgery, her blood pressure was 140/60 and her pulse rate was 124. Nasal oxygen was started, and an ice bag was placed on her abdomen. One and one-half hours after operation the patient was rational and vomited about 30 c.c. of dark fluid. Two and a half hours later the patient roused and voided 180 c.c., and then went back to sleep and rested quietly until morning.

There was a gradual rise in temperature until the afternoon of the second postoperative day when it reached 104° F. At this time 1,000 c.c. of 10 per cent glucose were given intravenously, and 30,000 units of penicillin every three hours was ordered. The penicillin was continued until the patient had a total of 630,000 units and the temperature became normal.

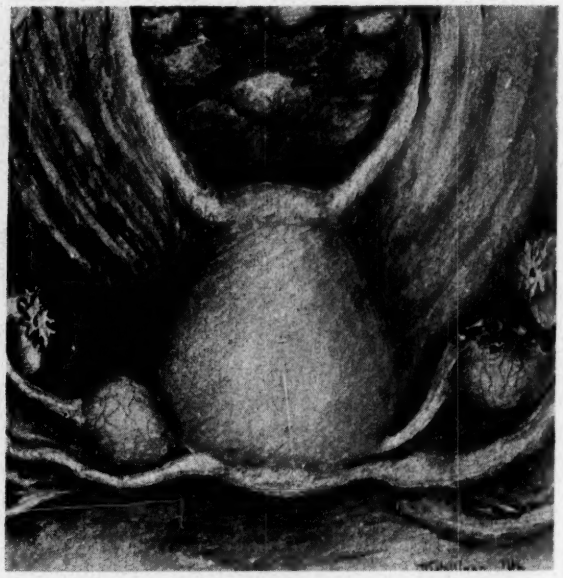

Fig. 1.

On the sixth postoperative day, the patient developed a very large herpes simplex which involved her upper lip, both ala nasae, and the right eyelid. These lesions were treated conservatively with zinc oxide ointment. The day following operation a catheterized urine specimen revealed the same findings as the preoperative specimens but a specimen on the second postoperative day was negative for albumin, and microscopically showed only 5 to 7 white blood cells per high power field. Four days postoperatively the urea nitrogen was 14 and the creatinin was 1.6. On the eighth day the skin sutures were removed and her incision had healed well. The patient was allowed out of bed on the tenth day and was discharged on the thirteenth in good condition. She was last seen twenty-three days after operation and at this time was asymptomatic. The incision had healed well and there was no herniation. The urinalysis and blood count, repeated at this time, was normal. The red blood count was 4,490,000.

The following pathologic report was received from the laboratory:

Gross: (A.) Specimen consisted of two Fallopian tubes, each approximately 10 cm. in length. One tube showed a dilatation due to an intramural hemorrhagic mass at the point of junction of tube and uterus. The mass was 2 cm. in diameter. Definite decidual tissue could not be identified in this tube. The distal portion of the tube was not remarkable.

(B.) The other tube showed a hemorrhagic mass within the lumen at a point 3 cm. from the uterus. This hemorrhagic mass was more suggestive of decidual tissue.

Microscopic: Section through both Fallopian tubes showed islands of chorionic villi in the lumen surrounded by hemorrhage and decidual cells. The walls of the tubes were partially lined by decidual cells, and were thickened by a diffuse cellular infiltrate consisting of lymphocytes, plasma cells, and a few polys. The walls were moderately edematous.

Diagnosis: Bilateral tubal pregnancy.

ANCYLOSTOMIASIS AND HYPOPROTEINEMIA COMPLICATED BY PREGNANCY

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DESPITE the fact that much has been written about the various anemias of pregnancy, a review of the literature reveals that little has been published regarding hookworm anemia, complicated by pregnancy. Although ancylostomiasis was common on Guam, the following case proved to be the most interesting, by far.

Case Report

The patient (C. R. C.), a 23-year-old, unregistered, single Chamorro woman was admitted to the Military Government Hospital on May 20, 1945. Despite the patient's protests to the contrary, her kinsmen called the ambulance because they felt she appeared to be ailing sufficiently for hospitalization. Upon arrival at the hospital, the patient walked into the ward. Her complaints were slight dizziness, pain in the region of the mons pubis, swelling of the legs which began two weeks prior to admission, and ammenorrhea for five months (the last menstrual period was December, 1944). In spite of the fact that the edema extended upward over the entire body, the patient had continued to perform all of her household duties. She had had no stool examination since 1940, nor had she taken helminthogogues. During the Japanese occupation her diet consisted chiefly of rice, fruits, and vegetables, since meat and milk were not available. After the Americans regained Guam, canned meats and powdered eggs were accessible, but the patient stated that she had consumed little of either.

Physical Examination.—The temperature was 98.8° F.; pulse 100; respirations 32; blood pressure 140/88. The patient was extremely pale and presented a generalized edema which pitted deeply on any part of the body. The eyelids were swollen almost closed. The patient seemed to be mentally sluggish and was virtually amnesic of the past few weeks.

The face was very swollen and waxy in appearance. The mucous membranes of the eyelids and mouth were extremely pallid. The tongue was pearly white and flabby. There were no cardiac murmurs or arrythmias. The lung fields were essentially negative; only a few moist râles were elicited at the bases, posteriorly. The breasts were moderately enlarged, and a small amount of colostrum could be expressed from the nipples.

There was a four-plus pitting edema over the entire abdomen, particularly over the mons pubis. The uterus extended one finger's breadth above the umbilicus. The fetal heart tones were distant and rapid. The skin over the lower part of the abdomen showed many pallid striae gravidarum. Pelvic examination was deferred because of the severe edema of the labia.

The skin was dry, pasty in appearance, and tense. There was a four-plus pitting edema of the lower extremities. The fingernails were colorless. The deep tendon reflexes were sluggish. The impression was that the patient had ancylostomiasis and hypoproteinemia, associated with a 22 weeks' gestation.

Laboratory Findings.—The blood drawn from the right antecubital vein resembled cloudy serum streaked with strands of brick-red dust. The very few red cells present rapidly precipitated to the bottom of the test tube. The hemoglobin determination (Sahli), done from blood drawn from the vein, was not recordable —"less than 2 grams." *The red blood cell count was 240,000.* The white blood cell count was *400.* A differential count was impossible because the blood smear

was too thin. The patient was group B. The Rh determination was not done since anti-Rh testing serum was not available. The urine examination was essentially negative.

Blood Transfusions.—Shortly after admission, 1,300 c.c. of citrated, cross-matched, group O blood was given, without any reaction. This was followed with 200 c.c. of serum albumin. The blood count, 15 hours later, showed the hemoglobin to be 22 per cent; red blood cells 960,000; white blood cells 9,200; differential smear: neutrophiles 79 per cent, lymphocytes 17 per cent, eosinophiles 4 per cent. The total proteins were 4.1 Gm. per 100 c.c. of blood. The presumptive Kahn was two plus.

The next day, eighteen hours after admission, the patient was given 1,000 c.c. of group O blood (uncross-matched) and 100 c.c. of serum albumin. Blood counts taken twenty-four hours later showed: hemoglobin 22 per cent (3.5 Gm.); red blood cells 1,020,000; white blood cells 11,200.

Hospital Course.—Besides blood transfusions, the patient was given 1 c.c. of liver extract intramuscularly, daily; ferrous sulfate grains X, three times a day; and multivitamin pills three times daily. She was placed on a high protein, salt-free diet.

The fluid intake during the first twenty-four hours was restricted to 1,000 c.c. by mouth. The output was not recorded, but the patient experienced marked diuresis following the serum albumin therapy, and, within forty-eight hours of admission, there was only a two-plus pitting edema. Absolute bed rest was maintained until the sixth hospital day when the patient was edema free. The total proteins on the eighth hospital day had risen to 5.8 Gm. per 100 c.c. of blood; red blood cells 3,170,000; hemoglobin 60 per cent; white blood cells 10,650; the differential smear revealed: neutrophiles 83 per cent, lymphocytes 5 per cent, eosinophiles 11 per cent, basophiles 1 per cent.

The stool specimen showed many ova of hookworm. Since tetrachlorethylene was unavailable, oil of chenopodium was given in 15 minim doses, every thirty minutes, for three doses. A stool examination one week later showed ova for hookworm, ascaris lumbricoides, and the larvae of *S. stercoralis.*

On the sixteenth day, the patient was discharged from the hospital with a hemoglobin of 72 per cent (10.5 Gm.) and a red blood cell count of 3,420,000, and was referred to the prenatal clinic. Ferrous sulfate therapy was continued. The admission weight was not recorded. The discharge weight was 135 pounds.

Prenatal Course.—During the next three months, on a diet enriched with canned milk, eggs, and cheese, the weight gain was seven pounds. The patient was seen every two weeks in the prenatal clinic until the eighth month; thereafter, she was examined every week. Tetrachlorethylene (3 capsules) was given at the seventh month. Mapharsen and bismuth were administered for latent yaws. Repeated blood counts revealed a gradual increase in the red count and hemoglobin. On August 13, two and one-half months after the hospital admission, the red blood cell count was 3,550,000, the hemoglobin 83 per cent (12.0 Gm).

Labor.—The patient was readmitted to the hospital on September 10, with premature rupture of the membranes. The blood picture at that time showed: red blood cells 3,870,000; hemoglobin 68 per cent (9.5 Gm.). Physical examination revealed the patient to be in excellent condition. The blood pressure was 110/80. There was no edema. The weight was 142 pounds. The uterus was almost term size, with the infant lying in the left occipitoanterior position, head partially engaged. The infant's weight was estimated to be 6 to 6½ pounds. Rectal examination revealed the cervix not effaced nor the os dilated. Liquor amnii definitely was escaping from the introitus.

Delivery.—Twenty-four hours after admission, the patient went into active labor and was medicated with 3 grains of nembutal and 1/100 grain of scopolamine. The latter was repeated in one hour. After eight hours of labor, the patient had a low forceps delivery under spinal anesthesia (70 mg. novocain). A median episiotomy was done. The blood loss was estimated to be 75 c.c. The infant was a 7 pound, 2 ounce boy, markedly asphyxiated. It gasped once and the cardiac impulse was palpable for twenty minutes. The usual methods of resuscitation failed and the infant succumbed. The umbilical cord was around the neck once, and it was observed that a loop had been caught in the left forcep blade. The infant appeared to be well developed. Autopsy examination revealed atelectasis.

Postpartum.—The patient's postpartum course was afebrile. A blood count taken one week after delivery showed: red blood cells 2,740,000; white blood cells 15,000; hemoglobin 48 per cent (7 Gm.). The blood Kahn was negative. A stool specimen was reported positive for *Endamoeba histolytica,* cysts of *E. coli,* ova of hookworm, ascaris lumbricoides, and *T. trichuria.* The patient was transferred immediately to the medical ward where therapy for helminths was instituted. One month later, she was discharged, free of "worms." A blood count at that time (Oct. 11, 1945) showed: red blood cells 3,900,000; hemoglobin 74 per cent (10.5 Gm). The patient was asymptomatic, and a pelvic examination revealed normal involution of the uterus.

Comment

It is interesting to note that the patient's complaints were relatively trivial compared with those one would expect from the clinical and laboratory findings. Our observations concerning ancylostomiasis astounded us in that the patients had very few subjective complaints. Most of them stated that they tired easily, experienced vertigo, and noticed some shortness of breath on exertion. Very few of them experienced syncope or extreme weakness. We concluded that the onset and progress of the anemia was so gradual that the patient adjusted himself to the condition, and was, therefore, able to live and work without much difficulty.

Dr. H. M. Zimmerman,[1] our pathologist, who performed the autopsies on many infants and children who succumbed to hookworm anemia, feels that the hookworm secretes an antigen which depresses the homopoietic centers, particularly the red-blood-cell-forming elements. Conversely, the white blood cells, especially the eosinophiles, are stimulated; consequently, most of the blood smears show an eosinophilia varying from 5 per cent to 33 per cent. Some writers[2] believe that the severe anemia is caused by the mechanical withdrawal of blood from the patient by the worms attached to the intestinal wall.

Some books on tropical medicine[2, 3] state that the red blood cell counts in patients infested with hookworm vary from one to three million, with hemoglobin readings varying from 20 to 40 per cent. This conclusion was verified in the thousands of Chamorros examined on Guam. The most severe anemias were found in infants, children, and pregnant women. Many patients in these groups had hemoglobin determinations of 2 to 4 grams. Despite multiple blood transfusions, many of the extremely morbid infants and children succumbed.

In almost every instance of edema associated with hookworm anemia, serum protein studies revealed evidence of hypoproteinemia. Investigators[2, 3] find that the plasma volume is increased, while the total blood volume is diminished. Blood cholesterol, serum proteins, and serum calcium determinations are low. These conditions are rectified simply by means of diet, calcium, blood transfusions, and serum albumin therapy.

During a two-year period (1932-1933), at the De Soysa Lying-in Home, Colombo, Ceylon, Wickramasuriya,[4] in a study of hookworm disease as a complication of pregnancy, reports a maternal and infant death rate of 27 per cent and 23 per cent, respectively. He states that ancylostomiasis was, by far, a greater menace to the expectant mother and unborn child than were puerperal sepsis, eclampsia, pyelitis, and postpartum hemorrhage. The majority of the sufferers of severe hookworm anemia succumbed to cardiac failure either during or after delivery. He further relates that abortions, miscarriages, and stillbirths were very commonplace. Furthermore, many young women were rendered unfit for motherhood either as a result of cardiac disability or defective renal function, or both. Evidently, many of the deaths reported were in unregistered patients who were admitted to the hospital in extremis. Since no mention is made of blood transfusion therapy, one would expect a high maternal death rate. The Chamorros on Guam were urged to register for prenatal care early in pregnancy; the severe cases of hookworm anemia were immediately hospitalized and given multiple blood transfusions. As a result of prenatal care, not a single mother succumbed in the 838 patients delivered during the interim of Dec. 1, 1944, to Dec. 1, 1945. It was noted in the early days of establishing the clinics that the incidence of abortions, miscarriages, and stillbirths was high. However, as a result of the commendable cooperation of the expectant mothers in attendance of the clinics, the gross fetal mortality rate for the year was only 5 per cent.

In the early days of the prenatal clinics, a survey of the stool examinations revealed that 95 per cent of the patients were infested with intestinal parasites, particularly hookworm and ascaris lumbricoides. At the end of one year, 73 per cent of the undelivered patients showed worm infestation. A survey of the treated delivered patients was not completed. Prior to the American invasion in July, 1944, helminthogogues had never been administered to pregnant women on Guam. They feared that the "worm medicine" would affect the unborn child or cause abortion. After prenatal clinics, twelve in all, were established over the island, every patient who had a positive stool was treated. Not a single patient aborted, miscarried, or delivered prematurely. Most of them averred that they felt much better. Certainly, the infants delivered from the treated group were healthier, and the likelihood of helminthiasis was reduced.

A question arose as to whether or not the hookworm larvae passed from the maternal circulation to the fetus. Therefore, the meconium was examined in a large number of newborn infants, with the result that all stools were negative for any type of parasite. The infants were infected shortly after birth because of unsanitary living conditions.

Without any doubt, the incidence of worm infestation was markedly increased during the Japanese occupation, since little or no medical attention was given the people of Guam, and they were forced to live under unspeakably filthy conditions. Several years of enforced public health principles will eliminate the extensive prevalence of parasitic infestation which still exists.

The views and statements in this communication are not necessarily accepted and confirmed by the U. S. Navy.

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GAS BACILLUS INFECTION PRIMARY IN THE UNBORN FETUS, WITH REPORT OF A CASE SPONTANEOUSLY OCCURRING AT TERM, THE MOTHER SURVIVING

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A NEGRO primipara (Case No. 17646), aged 23 years, was admitted to Maternity Center Clinic, July 6, 1943, in her third month of pregnancy. Her general health was excellent, she had had no abortions or operations, she showed no sign of vulval or cervical infection, smears were negative for gonorrhea, and the Wassermann was negative.

In January, her ninth month, she developed hypertension and albuminuria that increased notwithstanding home treatment so that on Jan. 20, 1944, she was sent to the hospital as a pre-eclamptic at term. Blood pressure was 170/115, and albumin was 2 plus. The fetal position was diagnosed as right occipitoposterior. Her nonprotein nitrogen was found to be only 28 milligrams.

After castor oil and an enema, pains began about 1 A.M., January 21. Two hours later, according to the nurses, the membranes appeared at the vulva and spontaneously ruptured. The patient was moved to the delivery room. After three hours, pains lessened and she was returned to her bed.

At 10 o'clock that morning, I found the head barely engaged, position right occipitoposterior, the fetal heart heard for what proved to be the last time, amniotic fluid draining away, the cervix only about 1 cm. by rectal examination with effacement estimated at 30 per cent, temperature normal, and blood pressure 170/90.

Through the rest of January 21 and 22, her labor was that of the usual occipitoposterior, with slow dilatation and ineffectual pains. Four per cent mercurochrome was instilled into the vagina four times, beginning at 9 P.M. on January 21. This was the only invasion of the vagina before delivery.

On January 22, the pelvis was confirmed as adequate by x-ray. That evening, her temperature rose to 100° F., but it was thought to represent only the stress of labor and dehydration. There was no other rise before delivery.

At 2:30 A.M., January 23, dilatation was complete and the head was bulging the perineum. Up to this time, no abnormality of the fetus, other than simple death, was suspected. At 3:30 A.M., the caput was in sight, and, much to our surprise, felt like a bag of water. No bone was palpable.

Believing it to be hydrocephalus, the scalp was clipped with scissors; necrotic brain tissue and gas burst forth under pressure, with an odor far more foul than *bacillus coli*. The contents of the cranial vault was completely liquefied. Though the bones of the vault were not palpable at this time, the pathologist later reported that the centers were still present.

Birth was accomplished without apparent damage to the maternal soft parts, other than an episiotomy.

The condition of the placenta was carefully noted, but, macroscopically, it showed no pathology. It was not sectioned.

The child's development appeared normal, and weight was estimated at 7 pounds. There was marked gaseous distention of the abdomen, and subcutaneous crepitation was definite in all limbs. The skin was discolored but not macerated.

The autopsy, by Dr. Arnold F. Straus, pathologist, showed: "Skin throughout grayish red with greenish discolorations, but not macerated. General subcutaneous crepitation, and evil odor. On opening, muscle tissue shows gas blisters. The pleural, pericardial, and peritoneal cavities, all show a small amount of hemorrhagic fluid. All organs showed a

dirty grayish red, discolored and cloudy. Direct smears from blood and liver were loaded with gram-positive rod-shapes. Cultures from blood and liver showed gas-forming and spore-forming gram-positive bacilli in buffered medium.''

Four hours after delivery, the mother's temperature was 104.6° F. A therapeutic dose of gas serum was ordered, but, through misunderstanding, a prophylactic dose of 1,500 units was all she received that day.

The next day, January 24, her temperature continued near 104° F., but she had no chill. Hemoglobin was reported 103 per cent, and red blood cells 5,100,000. A therapeutic dose of serum—*Cl. perfringens* 10,000 units and *Vibrion septique* 10,000 units—was given intravenously. Sulfanilamide, initial dose 3 grams with sodium bicarbonate, and 1 gram every four hours, was started. Penicillin was not then available.

On January 25, her second day, hemoglobin was 94 per cent, red blood cells 4,620,000, white blood cells 13,400, and polys 71 per cent. Through a bivalve speculum, a culture was taken from the cervix, after which 5 grams of sulfanilamide powder were placed in the vaginal vault. This treatment was continued twice daily.

Consultation with an obstetrician and a surgeon was obtained. They considered the case hopeless, and offered no suggestions as to treatment.

A blood culture taken on January 26 was negative.

During the first two days post partum, the patient had mild vomiting; during the third and fourth days, she had loose stools. The abdomen was moderately distended and tender. Intravenous glucose, 1,000 c.c. of 10 per cent, was given.

Her temperature remained between 102° and 104.6° F. for five days. It reached normal on the seventh day, and there was no further rise.

The episiotomy wound opened completely and was covered with a thick dirty-gray slough. Sulfanilamide powder cleared it promptly, and the wound healed by granulation.

Blood sulfanilamide reached its peak on January 27, 5 mg. per 100 c.c. On January 30 it was 4 mg.

The culture taken from the cervix on January 25 showed gram-positive gas-forming rods and capsules, hemolytic and nonhemolytic streptococci, *B. coli*, and *Staphylococcus albus*.

We were amazed to see this patient begin to improve. Treatment had not been strenuous, nor very prompt. However, she was discharged from the hospital February 5, her thirteenth day, comfortable, eating well, with blood pressure 130/80, fundus 4 cm. above the symphysis, and lochia scant and colorless.

One month later, at the clinic, she appeared in perfect health, the pelvis showed no inflammatory residue, and she was discharged.

Incidentally, she again became pregnant in three months. She carried to term and had a normal spontaneous delivery at home, under clinic supervision, in January, 1945. There was no morbidity this time.

Our theory regarding this case is that gas bacilli were carried into the vagina by sexual intercourse, which admittedly occurred as late as two days prior to admission to hospital. In the cervix, spores remained dormant until membranes ruptured forty-eight hours before delivery. Then, by some route, probably amniotic fluid, nostrils, and cribriform plate, they reached the meninges and brain of the baby. Brain tissue, more particularly dead brain tissue, being the best-known culture medium for the gas bacillus, there was time for the organism to flare into virulent activity and produce the pathology found. Also, some of the infected amniotic fluid may have been inhaled and ingested, infecting lungs and intestinal tract. The mother's tissues were not attacked before delivery, because up to that time she had no devitalized tissue. The placenta, too, appeared to be an effective barrier, for the mother's protection.

We were fortunate, here, in the comparative absence of mixed infection. As pointed out by Bysshe, the mixed infection probably multiplies the toxins and aids in their liberation.

Discussion

Authors seem to have agreed that devitalized tissue is fundamentally necessary for the *Clostridium welchii* to implant itself and propagate in sufficient numbers to initiate active infection.

May it not be that amniotic fluid is a satisfactory culture medium, and the particular medium that carries infection into the uterine cavity, in the absence of instrumentation and trauma? There seems to be very little written about amniotic fluid as a culture medium. If true, it would explain much about abortal and prenatal infections. Cosgrove and Barry discuss at some length the exact manner in which the gas bacillus, dormant in the cervix, may become active and reach the fetus, when there is no dead tissue present. In their case, as apparently in all others of this type, the membranes ruptured early. Progress of the infection upstream into the amniotic sac is probably aided by the contractions and relaxations of the uterus in labor.

What caused the baby's death, in our case? Was it maternal toxemia, interference with circulation in the cord, or the infection? Had the circulation ceased before it was attacked by gas organisms, or did gas bacilli attack a living baby?

In treatment, how much benefit was derived from the simple admission or air into the vagina twice daily for six days, when the sulfanilamide powder was introduced? This was admitting air to the focus of an anaerobic organism. Is this treatment entitled to particular credit?

Summary

1. The rarity of gas bacillus infection that is primary in the unborn fetus is noted.

2. A case of such infection following premature rupture of membranes at term is reported.

3. This fetus showed liquefaction of the brain and generalized gas infection, which had developed without giving symptoms in the mother.

4. The trauma of delivery promptly started active infection in the mother; life was threatened for seven days, followed by recovery.

5. Treatment consisted only of (1) serum, a prophylactic dose on the first day, and a therapeutic dose intravenously on the second; (2) sulfanilamide and soda by mouth, for seven days, but only to a blood concentration of 5 mg.; (3) sulfanilamide powder into vaginal vault, through a bivalve speculum, twice daily; and (4) supportive treatment of intravenous glucose.

6. Though the virulence of the strain probably was not maximum, recovery was unexpected.

7. The possible role of amniotic fluid as a culture medium that initiates the growth and spread of the infection in the absence of dead tissue is suggested.

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AN AID IN THE DIAGNOSIS OF FETAL POLARITY

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AN ACCURATE clinical diagnosis of the fetal polarity in the obstetric patient in labor is most important. Abdominal findings (position of the fetal heart, palpation of the fetal small parts, palpation of the upper and/or lower pole of the fetal axis) are often inconclusive because of: (1) the obesity of the patient, (2) the voluntary resistance and uncooperative posture, (3) the inferential character of the findings.

The patient in labor with a breech presentation offers a problem separate and apart from the same patient with the identical fetus presenting as a vertex. The greater efficiency of the vertex as a dilating pole is universally known and accepted. The vertex presentation with slight or moderate cephalopelvic disproportion often resolves itself following adequate labor, with molding of the head, and vaginal delivery is accomplished without great difficulty. The same head coming through the pelvis as the aftercoming head of a breech presentation offers an entirely different problem. No opportunity is afforded the head to become molded and accommodate to the pelvic configuration. As a result of the dystocia and the frequently difficult vaginal delivery, a disastrous result may be the eventuality to the baby and, at times, to the mother. The fetal mortality in breech presentation averages about 14.1 per cent (Hirst 20 per cent,[1] Curtis 13 per cent,[1] Williams 10-14 per cent,[1] Stander 13.1 per cent,[2] Beck 10 per cent,[3] DeLee-Greenhill 6-32 per cent,[4] Margaret Hague 11.2 per cent.[5] While the maternal mortality in breech presentation is not significantly different than with vertex presentation,[2, 4] the incidence and severity of perineal and soft tissue injury is materially greater.[1, 2]

Mindful of the necessity of making the clinical diagnosis of breech presentation more accurate and precise, the writer attempted to find some additional information that would be of assistance. No positive findings to assist in the diagnosis of breech presentation could be determined other than the well-known findings of: palpable vertex in the uterine fundus, fetal heart tones in one of the upper abdominal quadrants, absence of cephalic prominence over the symphysis, and palpation of a soft, compressible breech, rectally or vaginally.

These findings are adequate in the patient whose abdominal wall and voluntary posture permit satisfactory palpatory examination and whose cervix is sufficiently effaced and dilated to permit thorough palpation and exploration of the presenting pole, rectally. It was found, however, that upon rectal examination the presence of a thick lower uterine segment with an uneffaced, undilated cervix offered a rather difficult medium through which to confirm the presence of a breech or vertex over the pelvic inlet.

Stander has mentioned a "characteristic crackling sensation upon compressing the bones of the skull" obtained occasionally upon palpation of the

skull of a breech presentation through a thin abdomen.[2] This finding, when elicited, may be of positive assistance in the diagnosis of a breech presentation.

It was observed that if the presenting pole was steadied over the inlet by impressing the fundus from above by the external hand of the examiner, and the presenting pole explored through the lower uterine segment, the sensation of buckling, as if a derby hat were compressed, was felt if a vertex presented. This was noted through lower uterine segments that were thick, as well as through those that were thin. The palpatory sensation is similar to that described in the cephalic palpation of the rachitic skull with craniotabes.[6] The presence of this sensation indicates a vertex presentation. While this does not offer a positive assistance in the diagnosis of breech presentation, in a negative way, it has helped rule out the possibility of breech in numerous equivocal cases when x-ray was not immediately available and vaginal examination was not desirable.

It has been found that not all presenting vertices will give this sensation, but a great many will. One must be cognizant of the urgency for gentleness in the rectal exploration so that the buckling that is felt is a finding in the palpation rather than the result of denting of the fetal skull from a vigorous probing of the presenting fetal pole. The finding is offered merely as an adjuvant in the diagnosis of fetal polarity.

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DIABETES INSIPIDUS AND PRE-ECLAMPSIA

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THE following case is reported because it deals with a patient with long-standing diabetes insipidus, who became pregnant and developed a severe pre-eclampsia. With progression of the pre-eclampsia, the polyuria and polydipsia almost disappeared, only to recur gradually after delivery.

This patient, white, 27 years old, was first seen Nov. 25, 1944, with the usual presumptive signs of pregnancy. Her last period was July 20, 1944, which made her confinement date April 27, 1945. Her menarche occurred at 14 years of age, followed by scant, painful, three-day periods every thirty days.

Her past history is significant only as it related a tremendous thirst and comparable urinary output for over twenty years' duration. She placed her intake of fluids at as much as eight gallons in twenty-four hours. She urinated often—hourly during the night. A transfusion reaction when five years old was supposed to have been responsible for this condition. Due to previous experiences, she requested that her diabetes insipidus not be treated.

Physical examination was negative except the pelvis. The bladder was distended and the uterus was enlarged and gravid. Genitals were nulliparous. Generally she appeared healthy and well nourished. Her blood pressure was recorded at 120/75, and her weight was 121½ pounds. Serology was negative, her red blood count was 2.6 million, and hemoglobin 61 per cent, urine specific gravity was 1.004.

Her prenatal record shows an unusual persistence of nausea with some vomiting and increased nervousness and sleeplessness. In January, the sixth month, her blood pressure became elevated and varied between 140/90 and 185/115 until delivery. In February, the seventh month, water intake and output diminished greatly, and sweating became profuse day and night. Albumin was detectable from early March until delivery. A coincidental left facial paralysis developed in March also and gradually improved after several months. On March 16 she was hospitalized for control of the pre-eclampsia. According to hospital records, her intake and output (specific gravity 1.004) reached a new low in her memory of about one gallon in twenty-four hours. Because her fetus was quite small, she was dismissed five days later without induction of labor.

On April 16 the patient was again hospitalized because of severe pre-eclampsia. Prior to delivery her intake approached normalcy (about 1,500 c.c.), while the urinary output (specific gravity, 1.010) usually exceeded this by nearly 1,000 c.c. This discrepancy occurred in spite of the absence of clinical edema. On April 25 labor was induced medically, and after five hours of labor a 4½-pound immature baby was delivered spontaneously and lived. The postpartum course was uneventful except for slight morbidity. On the third postpartum day intake and output again exceeded one gallon each. By August, four months post partum, her intake and output (specific gravity, 1.004) exceeded two gallons daily. Her blood pressure has been normal since her examination six weeks after delivery.

This case of diabetes insipidus and pregnancy provokes some interesting conjectures. The development of a severe pre-eclampsia makes this case more

unusual. Disappearance of polyuria and polydipsia during pregnancy and their return afterward are not unusual features. The persistence of nausea and vomiting and the development of pre-eclampsia in the presence of this syndrome would suggest that copious fluids are not always adequate treatment for these complications of pregnancy. The simultaneous regression of diabetes insipidus and onset of pre-eclampsia might lend support to the antidiuretic theory of this toxemia. On the other hand, since the diuresis was never completely overcome, we might assume that pre-eclampsia is the cause rather than the result of the antidiuresis. The immaturity at term of an otherwise normal infant is interesting.

COMBINED PROCEDURE FOR ANTEROVERSION OF RETROVERTED UTERI

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REPLACEMENT of the retroverted uterus is not always possible when bimanual manipulation is performed in the lithotomy position. Attachment of a tenaculum to the cervix facilitates replacement in certain cases, but its use is undesirable for pregnant uteri. Correction in the knee-chest position may also be impossible, or if it is accomplished, the uterus falls back when the patient is subsequently re-examined for insertion of the pessary in the lithotomy position. Under such circumstances further attempts are either given up entirely, or replacement is accomplished under general anesthesia. The importance of the correction of malpositions of the uterus is beyond the scope of this article, yet the improved chances of conception, prevention of spontaneous miscarriage, relief of nausea in pregnancy, alleviation of backache, and treatment of the incarcerated pregnant uterus are acceptable indications. The contraindications are: absence of symptoms in nonpregnant women, vaginitis, and medical indication for a contraceptive diaphragm.

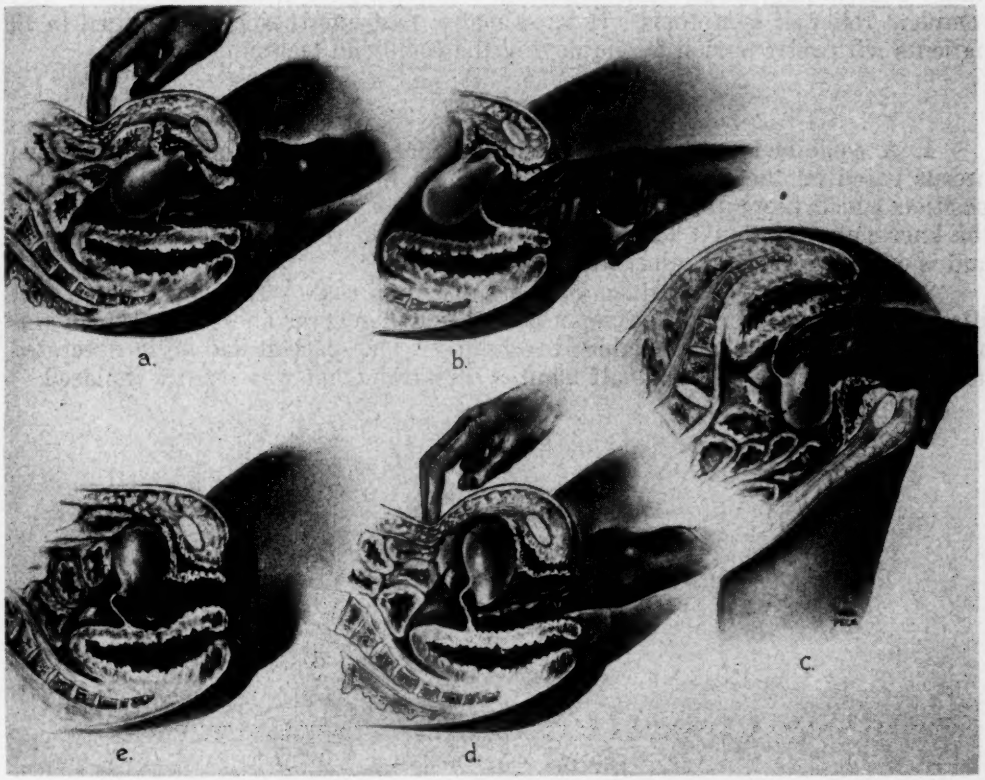

Fig. 1.—Technique of the combined procedure for manual replacement of a pregnant retroverted uterus.

The following technique has given uniformly excellent results at the Army Air Forces Regional Hospital at March Field, California:

1. The diagnosis of retroversion uteri having been made vaginally in the lithotomy position and the indications for replacement having been fulfilled; a well-fitting Smith-Hodge pessary is inserted (Fig. 1, *A*, *B*).

2. The patient then assumes an erect position on a low stand situated at the examiner's end of the examining table, turns about face, places the knees on the edge of the table and assumes the knee-chest position.

3. Re-examination allows the vagina to expand with air. Downward pressure is made on the lateral bars of the pessary, alternating with backward pressure on the cervix, while the patient coughs several times. These measures usually produce anteroversion of the uterus (Fig. 1, *C*).

4. The patient falls slowly into the prone position momentarily and then rolls over into the original lithotomy position.

5. Re-examination and any further manipulation for completion of the uterine replacement is carried out per vaginam (Fig. 1, *D, E*).

6. Routine instructions as to douches and revisits are given.

Fifty-five patients with retroversion uteri in early pregnancy, or not pregnant have been treated with the above technique. No failures have occurred, probably because no fixed retroversions have been encountered. One patient had an incarcerated uterus with a three and one-half month gestation which resisted the usual method of replacement since manipulation was painful. She was suffering from severe sinusitis which was a contraindication for replacement under general anesthesia. The combined technique gave an excellent result, with complete relief of symptoms. It is estimated that anesthesia was avoided in 10 patients with retroversion by employing the combined technique.

Summary

1. A combined procedure is described for replacement of the retroverted uterus based on the preliminary insertion of a well-fitting pessary in lithotomy position which keeps the uterus from falling back after it has been replaced in the knee-chest position. The use of a tenaculum in replacement is unnecessary, and is often undesirable, especially in pregnancy.

2. The procedure has given good results in 55 cases. It was estimated that 10 cases would have required replacement under general anesthesia, which was obviated by the use of the combined technique. One patient had an incarcerated uterus with a three and one-half months' gestation that was readily replaced.

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MODIFICATION OF THE ERICSON AND JOHNSON RESUSCITATOR

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THE following modification of the widely used Ericson and Johnson resuscitator was devised with the idea of facilitating its use. Frequently one gets the impression, when using certain devices, that the designer had not actually used the device under normal operating conditions. In the case of the Ericson and Johnson resuscitator, we found that the relation of the tubing to the machine and to the mask made it needlessly difficult to hold the mask snugly and

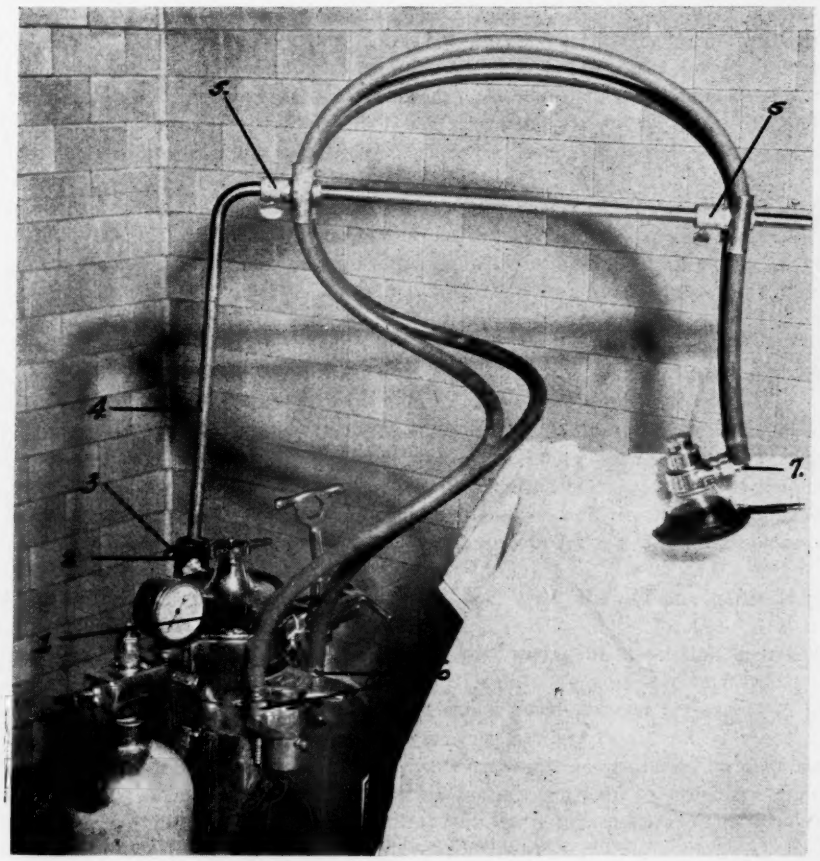

Fig. 1.

comfortably against the infant's face; and we also found a tendency, because of the weight and stiffness of the tubing, for the mask and tubing to fall to the floor whenever it was laid aside temporarily. It was with these problems in mind that this modification was developed.

Fig. 1 is to a large extent self-explanatory. A collar (*1*) was made to slip over the machine and fasten with thumbscrews. Welded to this collar is a sleeve (*2*) through which passes an L shaped rod (*4*), which can be held at any de-

sired level by a thumbscrew (*3*). On the horizontal member of the rod there are two movable sleeves (*5*), each of which is welded to two other sleeves at right angles, and through these pass the heavy tubing to the mask. The tube connections to the machine (*6*) have been inverted so they now point up instead of down, and right angle elbows (*7*) have been added to the mask so that it normally remains in proper relationship to the face.

Friction and tension cause the mask to remain at whatever level it is set, and this enables one to use the machine for continuous oxygen by simply moving the baby's head against the side of the crib and holding it there with a small sandbag, and then setting the machine on inhalation and adjusting the mask to the baby's face.

The modification is inexpensive and can be made by almost any mechanic. The connections at (*6*) were found to be soldered in and had to be heated in order to invert them.

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Department of Reviews and Abstracts

Selected Abstracts

Sterility, Fertility, Contraception

Halliday, J. L.: Psychosomatic Medicine and the Declining Birth-Rate, Lancet 248: 601, 1945.

Halliday's purpose of his article was to suggest the value of applying a psychological approach to the problem of declining birth rate.

The author insists that behavioral sterility, increasing frequency of practice of birth control, usually by coitus interruptus, is an expression of neurotic anxiety. This induced sterility could often be related to the obsessional characteristics, in that, persons with such a rigid character structure tended to experience upsetting events, as childbirth and children, as a threat to the routine but precarious design for living in a dangerous and disturbing war period.

The writer is of the opinion that birth rate represents a sound index of psychological health. Between 1870 and the recent war periods, mass unemployment, financial crisis, increasing competition, decline of active religious faith, a desire for personal safety, and a preponderance of other as unfavorable factors occasioned an increasing social disintegration provocative of a declining birth rate. If the fertility rate (England and Wales) of 1870 were to be considered as 100 per cent, the drop in fertility by 1900 (the mildly anxious generation) was 25 per cent, and the drop by 1930 (the second and definitely anxious generation) was 59 per cent.

Halliday illustrates his suggestions for therapeutic standards in the national attempt to alleviate parental anxiety—that every mother receive for each child in its early formative years (up to the age of 3 or 5 years) everything that is required—food, clothes, perambulators, go-carts, baby chairs, utensils—everything—without charge and irrespective of social class. This positive step would relieve parental anxiety and provide a sense of belonging to the community.

If added nursery facilities were available *and used,* the present generating neurotic parents would be relieved of further tensional loads.

Other examples of therapeutic measures to treat social disintegration include the choice of scientific selection for pupils in schools in contrast to aggressive competition; vocational guidance; compulsory labor camps or their equivalent; and "social security" in its psychological sense—i.e., security against preventable neurotic anxiety.

Halliday concludes that only such therapeutic measures as are based on understanding of the primary etiological relevance of psychosocial factors can help to provide a generation of young persons less inhibited by neurotic anxiety and, as a consequence, socially more healthy, psychosomatically less incapacitated, and biologically more fertile. C. E. FOLSOME.

Barton, Mary, and Wiesner, B. P.: Waking Temperature in Relation to Female Fecundity, Lancet 11: 663, Nov. 24, 1945.

In fecund women the body temperature on waking in the morning varies with the phases of the menstrual cycle. A relatively high temperature is characteristic of the premenstrual phase and it persists after conception. Persistent low temperature excludes the diagnosis of pregnancy. The diphasic temperature cycle may persist in cases of amenorrhea, but more commonly amenorrhea is characterized by a monophasic waking temperature record. Certain types of infecundity are associated with absence of the high temperature phases.

The transmission from the low to the high temperature phase coincides with the ovulatory phase. The occurrence of this shift does not constitute a proof of actual ovulation. The use of the temperature record in the timing of intercourse and for other proceptive purposes is described. The waking temperature may also be employed in determining the postovulatory period during which conception will not take place. CARL P. HUBER.

Mateos Fournier, Manuel: Artificial Insemination, Prensa méd. mex. **10**: 13, 1945.

The author discusses the possible causes of sterility in the two partners of a childless union. If artificial insemination is found advisable, it is necessary first to fix the probable date of ovulation, which is fourteen days before the next menstruation in the woman with regular cycles. In the irregular woman, the minimal and maximal cycles are observed for a few months, the fourteen days subtracted, and the average is used, giving two or three monthly inseminations on the probable dates. The survival of the ovum is about twelve hours, and it is therefore difficult to obtain a satisfactory result from insemination; hence the procedure has to be repeated several times.

Simultaneously, the woman is submitted to a treatment of stimulating ovulation by means of extracts of the anterior lobe of the hypophysis, and the husband is advised not to have intercourse for several days preceding the insemination. In some cases he is also given hormonal extracts to stimulate maturation of his sexual elements.

The semen must be obtained by masturbation and deposited in a dry, sterilized glass container, such as a Petri dish which is then floated in a tray with some tepid water. When it is absolutely impossible to collect semen in this way, it is taken from the vagina immediately after coitus. In cases of oligospermia, the semen is centrifuged and the precipitate used. Insemination offers no difficulties, and the site selected for it may be vaginal, cervical, uterine, or tubal, depending on the findings of the case. In intrauterine maneuvers, the greatest care must be taken to avoid bleeding and contractions which may expel the semen. For the same reason, only one or two drops of the fluid are introduced. Sometimes, especially in sensitive women, antispasmodic medication is administered before and after the maneuver. A short rest on the operating table and bed rest for several hours at home are recommended. Over-all success of from 25 to 30 per cent can be expected. J. P. GREENHILL.

Gynecology

Kovacs, F.: The Significance, Diagnosis, and Treatment of Female Genital Tuberculosis, Monatschr. f. Geburtsh. u. Gynäk. **116**: 183, 1943.

The author encountered 191 cases of tuberculosis of the female genitalia in his private practice. Hence this disease is much more common than is generally appreciated. In 60 per cent of the cases, sterility is present. The most important diagnostic procedure is curettement and examination of the endometrium. In 60 per cent of the cases of genital tuberculosis, the uterine scrapings will reveal the disease. Hence this diagnostic measure should be used more widely. Likewise, curettement should be performed in all cases of sterility and menstrual disturbance. A careful curettement entails no danger of spreading the disease.

The conservative treatment of genital tuberculosis has not proved effective. Hence the author recommends early laparotomy as the best treatment. This form of therapy quickly eliminates the source of infection. In early cases, the ovaries need not be removed. Removal of the uterus is not a sacrifice, because these women are sterile anyway. The presence of pulmonary tuberculosis is not a contraindication to operation.

J. P. GREENHILL.

Hodgson, J. E., Dockerty, M. B., and Mussey, R. D.: Granulosa-Cell Tumor of the Ovary, Surg., Gynec. & Obst. **81**: 631, 1945.

The authors present 62 instances of granulosa-cell tumor occurring in the Mayo Clinic from 1910 to 1944. This comprises 1.63 per cent of 3,800 ovarian tumors seen during that

period. The most common symptom was uterine bleeding, although enlargement of the abdomen and amenorrhea were also commonly present. Urinary estrogens were demonstrated in one postmenopausal case. They disappeared twenty-four hours after operation. Further presumptive evidence of hyperestrinism was indicated from the frequent presence of endometriosis, uterine hypertrophy, fibromatosis and proliferative endometrium. Secretory endometrium was found in three cases, each showing luteinization of the tumor; however, twelve of the luteinized tumors did not show similar changes in the endometrium. Pathologically the tumors were of a low order of malignancy. Twelve cases showed a mixture of granulosa- and theca-cell elements.

There were five possible recurrences in the series. Four of these failures were accounted for by the performance of conservative operations on postmenopausal patients. It was therefore recommended that total hysterectomy and bilateral oophorectomy be the operation of choice in the older group. Less radical procedures seem to be indicated in younger women. Insufficient information was obtained from the series on the use of radiation, but it was suggested that this form of therapy may be of some value. L. M. HELLMAN.

Miller, Hilliard E.: The Rupture (Intraperitoneal, Intraintestinal and Intravesical) of Suppurative Pelvic Masses, New Orleans M. & S. J. **98**: 115, 1945.

A review of 44 cases of pelvic masses which ruptured spontaneously into the peritoneal cavity are presented. The most important factor in the occurrence of this accident appears to be trauma: directly by a blow or pelvic examination; and indirectly, following lifting, etc. The clinical picture is of two types: either of shock, or that of a spreading peritonitis (chills, fever, increasing pain, and rigidity). From a diagnostic standpoint, the previous knowledge of a pelvic mass followed by its disappearance with the above symptoms is most helpful. In the author's series of cases, the correct diagnosis was set down in only two of the 44 cases, which fact should make the physician consider this a diagnostic possibility more frequently. Removal of the infected adnexa is stated to be the procedure of choice. There is no specific statement made as to whether abdominal or cul-de-sac drainage from below was used in a review of cases. In some, the latter procedure (cul-de-sac drainage) might prove most useful. Routine cul-de-sac needling would certainly be helpful. No mention is made of the use of penicillin. Though cultures are generally sterile in such masses, when pneumococci, staphylococci, or streptococci are obtained, penicillin should be valuable. Prognosis is generally fatal without operative interference.

JEROME SHAPIRO.

Bryson, Elizabeth: The Psychosomatic Approach in Gynaecological Practice, Practitioner **155**: 378, 1945.

In 4,000 women patients seen in a given period in a private medical practice (without contract work or hospital appointment), there were 1,233 patients considered to be suffering from conditions in which both physical and psychical factors were involved, including 200 with gynecologic symptoms. In these two groups, there were 40 cases of definite psychosis, requiring psychiatric treatment, and 67 cases of organic disease requiring major surgery. But in the large number of cases between these two extremes, the treatment of the patient falls within the sphere of the general practitioner; to deal properly with this work, the practitioner must be specially equipped. He must accept the patient as a human being and deal with each patient individually and personally; this includes the acceptance of the psychologic difficulties that are causing or aggravating the state of "dis-ease." This involves listening to the patient's story, and acceptance of the psychosomatic approach to illness. Symptoms must be assessed in relation to the patient's personality; the presenting complaint may then be treated, but only with "constant awareness" of the psycho-physical interaction. This work requires not only a knowledge of physical medicine on the part of the physician, but also an understanding of psychopathology and a degree of analytical insight. With this approach, and care to avoid either physical trauma (as by unnecessary surgical procedures) or psychological trauma, most patients can be satisfactorily treated, and the others can be brought to the care of a specialist without undue delay. In the author's experience, as his "psychological sensitivity"

in dealing with women patients increased, minor operative procedures, such as curettage or dilatation (for dysmenorrhea) became increasingly unnecessary. The gap between the practicing physician and the psychiatrist must be bridged, but, in the author's opinion, this can best be done by enlarging the sphere of the practitioner. The family physician has the advantage of close contact with the patient and firsthand knowledge of family peculiarities and tendencies. He also sees the patient early enough, in the curable stage, before the family reactions have become fixed and irreversible, but, to effect a cure in this stage, he must have "the requisite interest and knowledge."

Schaub, Isabelle G., and Davis, James E.: The Significance of Streptococci Isolated From the Female Urinary Tract, Bull. Johns Hopkins Hosp. 77: 372, 1945.

The authors summarize the article as follows:

The histories of 500 patients from whose urine specimens streptococci were isolated have been carefully studied from a clinical standpoint, and conclusions reached in regard to the significance of the organisms.

Streptococci were found to be the sole cause of clinical disease in 25.2 per cent of the cases reviewed, and involved with other organisms in 28.8 per cent. In a total of 54 per cent of the cases, therefore, they were regarded as etiologically significant. In 6 per cent of the clinical cases studied, the role of the streptococcus was doubtful.

In 40 per cent of the patients from whose urine streptococci were isolated, no clinical evidence of urinary tract disease could be found in the history. The significance of the presence of streptococci in this high percentage of cases is discussed.

The relative occurrence of the various streptococci with *Escherichia coli* was studied and it was determined that the alpha and gamma enterococci were involved with *E. coli* in a significantly higher percentage of cases than the other streptococci with the exception of the gamma streptococci. C. O. MALAND.

Hardy, Harriet L.: The Clinical Significance of Data Accumulated in the Medical Care of Young Women, New England J. Med. 233: 811, 1945.

One of the purposes of this paper is to point out the wide range of physiologic variations that are possible among normal young women. The blood pressure readings in 1,000 college women between the ages of 16 and 22 years are recorded. Seldom, if ever, is it found that a low blood pressure reading and fatigue are directly related. A study of the white blood cell counts in the menstrual cycle revealed that for practical purposes of differential diagnosis, there was found in this study no suggestion that the white cell count undergoes a physiologic shift at any time in the menstrual cycle.

From this study it is concluded that since red cell counts and hemoglobin levels slightly lower than normal are apparently not related to fatigue, menstruation or infection, and produce no other symptoms, the body is able to manage efficiently with what has been considered to be less than the normal blood level. The author advises treatment, however, for an iron deficiency. JAMES P. MARR.

Labor, Management, Complications

Bret, J., and Deplus, J.: Obstetrical Consequences of Uterine X-ray Therapy. Frequency of Abortion and Cervical Dystocia, La Presse médicale 53: 255, 1945.

The authors studied the effects of radium therapy on subsequent pregnancies and labors. Regardless of the dose of radium used it produces sclerosis, particularly of the cervix. Because of this sclerosis, operative interference at the time of labor is necessary in 60 to 70 per cent of women who conceive after radium treatment. Furthermore, the sclerosis which also effects the uterine endometrium may result in disaster. Among 34 pregnancies in 23 women who became pregnant after irradiation, there were nine abortions and six premature labors. The 34 pregnancies yielded only 12 living children (36 per cent). The fetal deaths were by

no means all due to operative intervention. Some of them were born dead or were macerated. There were no fetal malformations in this group.

In the women who continue to term, premature rupture of the membranes is almost the rule. The membranes and placenta may adhere to the decidua in the lower uterine segment. In 50 per cent there are disturbances in the contractions of the uterus. Cervical dilatation reaches a certain point and then stops. These occurrences along with fetal death often lead to amniotic infection which is usually serious. In many cases the cervix must be incised and forceps used, often with disastrous results for mother and baby. In some cases embryotomy must be performed. Sometimes even this is impossible, and the entire uterus must be removed in one piece. J. P. GREENHILL.

Chanal, G.: Different Methods of Inducing Labor. The Medical Method and Its Results at the Geneva Maternity, Monatschr. f. Geburtsh. u. Gynäk. **119**: 69, 1945.

At the Geneva Maternity, Stein's medicinal method of inducing labor is used. The procedure carried out is as follows: the patient is given 60 Gm. of castor oil in one dose, 1 Gm. of quinine sulfate given four times at half-hour intervals, and 10 Voegtlin units of thymophysin, given three times at half-hour intervals. If labor pains are inadequate, three drops of Basergin are given every half hour for a maximum of 18 drops.

Forty-seven cases treated by this procedure were analyzed. In 87 per cent the therapy was successful. The fetal death rate was 6 per cent, but only one of three fetal deaths can be attributed to the induction of labor. There were no maternal deaths, and the morbidity rate was 10 per cent. J. P. GREENHILL.

Colmeiro-Laforet, C.: The Diagnosis of Rupture of the Amniotic Sac, Rev. espan de obst. y ginec. **2**: 99, 1945.

In reporting 450 tests of the acidity of the vaginal fluid by means of indicator paper, the author found that 95 per cent were in the normal range of acidity. Marked deviations from the normal range were found in cases of premature rupture of the amniotic sac.

J. P. GREENHILL.

Newborn

Vahlquist, Bo: Serum Iron and Serum Bilirubin in Congenital Anemia of the Newborn and Icterus Gravis Neonatorum, Upsala Läkareförenings Förhandlingar Ny Foljd. Femtionde Bandet 183, 1945.

The author gives a brief but clear résumé of the importance of the Rh factor determination, and also stresses the fact that the Rh mechanism does not cover all cases of congenital anemia of the newborn and icterus gravis neonatorum.

His present study is based on four patients with congenital anemia of the newborn and five patients with icterus gravis neonatorum. The serum iron and serum bilirubin content are noted in each case using the Jendrassik-Cleghorn method. He discussed the value and limitations of the Van den Bergh test, and has drawn a conclusion that in the newborn the Van den Bergh test is of no assistance in differentiating between hepatogenic and hemolytic jaundice. His results are discussed in this most informative article. JAMES P. MARR.

Wilmer, Harry A.: Two Cases of Periarteritis Nodosa Occurring in the First Month of Life, Bull. Johns Hopkins Hosp. **77**: 275, 1945.

The author summarizes the article as follows:

Two cases of periarteritis nodosa, one dying at ten days of life and the other at thirty-seven days, are reported as the youngest cases in the literature. In one case there was an umbilical infection; in the other there was a large inflammatory-necrotic mass involving the right adrenal containing large numbers of unidentified cocci.

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Symptoms of vomiting, abdominal pain, edema, and purpura, together with fever and leucocytosis were manifest in the first case. Vomiting, dyspnea, pallor, and leucocytosis characterized the clinical picture of the second case. In both instances the disease ran a fulminating course, and the diagnosis was not suspected before autopsy. C. O. MALAND.

Albaugh, C. H.: Congenital Anomalies Following Maternal Rubella in Early Weeks of Pregnancy, J. A. M. A. 129: 719, 1945.

Nine cases of congenital abnormality in the infant following an exanthem in the mother in the early weeks of pregnancy are herewith reported. The pathologic lesions associated with rubella are reviewed. The importance of this problem from a public health point is stressed. Various public health measures for control are enumerated. The most common lesions in infants born of mothers who contracted rubella during pregnancy are cataracts, cardiac septal defects, patent ductus arteriosus, deaf mutism, and microcephaly. Nearly all of the infants are poorly developed and present a feeding problem. WILLIAM BERMAN.

Kendig, Edwin J., Jr., and Fiske, Russel H.: Penicillin Ointment in the Treatment of Impetigo Neonatorum, J. A. M. A. **129:** 1094, 1945.

In 14 cases in which penicillin ointment had been used there were no new lesions after the treatment had been in effect for forty-eight hours. After a maximum of three days all the lesions appeared to be dry and healed. In three instances, however, there was a recurrence of the condition after the patient had been home from the hospital more than one week. Each recurrence was after treatment had been discontinued and baths had been started.

WILLIAM BERMAN

Bloxsom, Allan: Penicillin Locally in the Eyes of Newborn Infants to Prevent Ophthalmia Neonatorum, J. Pediat. **27:** 447, 1945.

An additional case of gonorrheal ophthalmia neonatorum developed after the use of a silver preparation in the Credé method of prevention. Four drops (250 units per cubic centimeter) of penicillin was instilled in each eye every four hours. This occurred in a nursery of twenty infants having been exposed to a possible gonorrheal conjunctivitis, and resulted in no further spread of the infection in the nursery.

The result suggests that penicillin locally can and should be used as a specific prophylactic agent in the Credé method of prevention of ophthalmia neonatorum.

JAMES P. MARR.

Harris, Evelyn S., and Platou, Erlin S.: Pyopneumothorax in a Premature Baby Successfully Treated With Penicillin, Am. J. Dis. Child. **70:** 226, 1945.

The authors report a case of pyoneumothorax seen in a premature infant seven days after its onset. It appeared that sulfamerazine was failing to influence the course of the disease. Penicillin was given over a period of fifteen days.

The possibility and early recognition of pulmonary infection following atelectasis in premature infants should be emphasized. JAMES P. MARR.

Freud, Paul, Rhodes, Adrian W., and Weisz, Albert: Hereditary Skin Defect in the Newborn Infant, J. Pediat. 27: 591, 1945.

The authors report an interesting case of hereditary skin defect of the scalp in a newborn. For the first time, the same defect in the same location was also found in the parent. JAMES P. MARR.

Vinson, Porter P.: Cardiospasm in the Newborn, J. Pediat. 27: 565, 1945.

The author defines cardiospasm as persistent dysphagia, with x-ray evidence of obstruction to food at the cardiac end of the esophagus without organic stenosis. He reports such a case, and stresses the value of concentrated food orally and adequate amount of fluid subcutaneously as the treatment of choice. JAMES P. MARR.

De La Villa, L., and Nieto, J.: Study of the Deviations From the Normal Weight-Curve of the Newly Born and an Investigation of Their Causes, Rev. espan. de obst. y ginec. 2: 11, 1945.

The authors observed 1,500 newborn living children for at least ten days after birth and found 204, or 13.9 per cent, with deviations from the normal weight curve. The deviations were classified in seven distinct curve types. The curve of greatest frequency, 26 per cent of the total deviations, represented a prolonged initial decline of weight, and a slow recovery. The most marked curve of deviation which showed no recovery of weight included 8.8 per cent of the total deviations, and included the three patients which did not survive. The illnesses of the mother which were correlated most closely with these deviations were infections and heart disease; other pathologic factors were premature labor, congenital weakness, syphilis, intracranial hemorrhage, and jaundice. It was not possible to establish any correlation between these deviations and the type of nourishment of mother or child.

J. P. GREENHILL.

Pregnancy, Complications

Burch, A. E.: The Association of Erythroblastosis Foetalis and Accidental Antepartum Hemorrhage, J. Obst. & Gynaec. Brit. Emp. 52: 463, 1945.

All cases of antepartum hemorrhage occurring at St. Alfege's Hospital between February and June, 1945, were studied for Rh factor. In six cases of placenta previa, the Rh reports are available for only five, and in all these the patient was Rh-positive. In five cases of accidental antepartum hemorrhage, the mother was Rh-negative and the father Rh-positive; in one other case of accidental antepartum hemorrhage, the mother was Rh-positive, and in another both mother and father were Rh-negative. In one case of antepartum hemorrhage, placental insertion not determined, the mother was Rh-positive. Thus five out of ten of the mothers who had accidental antepartum hemorrhage were Rh-negative with Rh-positive husbands; and in three of these women anti-Rh agglutinins were demonstrated in the blood. In the three cases in which the patient was delivered soon after the occurrence of the hemorrhage, there was one child with jaundice who recovered without transfusion, one with gross hydrops, and one stillbirth, possibly as a result of the course of labor. In the two cases in which the patient was delivered some weeks after the occurrence of the hemorrhage, the fetus in each case was stillborn, macerated, and of a size indicating death at the time of the onset of bleeding. In two of the cases with Rh-positive mothers, the Rh genotypes were determined; the mothers were found to be Rh_2 rh and Rh_1 rh, and the children Rh_1 Rh_2 in each case so that it is possible that less common antibodies were present in the mothers, but this was not demonstrated. It is also noted that two of the three cases of erythroblastosis fetalis occurring in six months at Queen Charlotte's Hospital, there was premature separation of the placenta with antepartum hemorrhage.

While this series of cases is small, the findings suggest that women in whom isoimmunization can occur are abnormally prone to accidental antepartum hemorrhage, and that the resulting damage to the placenta may be a factor in the transmission of antigen and antibody. In some cases there seems to be an association between the time between bleeding and delivery and the severity of the erythroblastosis and the titer of the agglutinins. The risk to the baby from erythroblastosis in such cases may be greater than the risk from prematurity, so that induction of labor rather than expectant treatment may be indicated, but whether this is the case is as yet impossible to say. Since women with antepartum hemor-

rhage often require blood transfusion, there is evidently danger of incompatible transfusion, except in institutions where Rh tests are made on all expectant mothers, or where there is a blood bank of only Rh-negative blood. HARVEY B. MATTHEWS.

Davis, L. J., and Forbes, William: Thiouracil in Pregnancy—Effect on Fetal Thyroid, Lancet 11: 740, 1945.

The authors report the case of a 21-year-old woman who had had one previous normal pregnancy, following which she developed evidence of thyrotoxicosis. She was started upon treatment with thiouracil, 600 mg. being given daily. Following successful therapy the dosage was reduced to two hundred milligrams daily and continued at this dosage level of five and one-half months, at which time she became pregnant. The dosage was further reduced to two hundred milligrams on alternate days. During the sixth month of pregnancy she complained of a severe headache which persisted for two days, and at which time she suddenly became cyanosed, collapsed, and died.

Examination of the thyroid gland of the fetus revealed it to be enlarged and hyperplastic as compared with a presumably normal gland from a premature infant, and it showed histologic evidence of considerable functional activity. It resembled the gland of an adult receiving too much thiouracil.

The authors concluded that administration of thiouracil to pregnant women, and probably to nursing mothers, demands caution. CARL P. HUBER.

Lagercrantz, Carl: Electrophoretic Analysis of Serum in Pregnancy and in Pregnancy Toxemia, Upsala Lakareforenings Forhandlingar 117, 1945.

Electrophoretic analysis of serum from nonpregnant, normal pregnant, and pregnant women with toxemic symptoms have been performed. The analysis showed

1. The x- and B-globulins increase both relatively and absolutely during normal pregnancy.
2. The albumin and total protein decreases during normal pregnancy.
3. Women with toxemia have both a relatively and absolutely larger x-globulin than normal patients.
4. There is no significant difference in the electrophoretic patterns of umbilical cord serum after a normal pregnancy and after a toxemic one. Umbilical cord serum shows small x- and B-globulins.

An account of earlier work on x- and B-globulins is given, and the probable nature of the raised x- and B- globulins during pregnancy and in cases of toxemia is discussed.

JAMES P. MARR.

Gosende, J. C., and Sandiano, R. O.: Chorea and Pregnancy, Bol. Soc. de obst. y ginec. de Buenos Aires 23: 798, 1944.

The authors report a case which they consider to be true chorea of pregnancy. The disease appeared between the seventh and eighth months of pregnancy in an 18-year-old primipara. A detailed study of the heredity, family, and individual history revealed no record of predisposing causes. The authors maintain that true chorea of pregnancy may occur when the toxins of pregnancy affect a susceptible patient. J. P. GREENHILL.

Monckeberg, C.: Hypertension in Pregnancy, Rev. méd. de Chile 73: 193, 1945.

The author finds that, while in normal pregnancy arterial pressure is normal, a slight increase during the latter part of the period is also normal, and during labor increased blood pressure due to effort is to be expected. Otherwise all cases of hypertension during pregnancy must be considered pathologic, either a chronic state temporarily aggravated, or an acute state produced by the pregnancy and by the complex glandular disturbances not yet well understood. J. P. GREENHILL.

Pregnancy, Physiology

Koloszynski, F. W.: A Short Study of Histaminase Activity During Pregnancy, J. Obst. & Gynaec. Brit. Emp. **52**: 426, 1945.

A method for the quantitative estimation of serum histaminase was worked out from the Kapeller-Adler test based on a qualitative method in which H_2O_2 produced by the action of histaminase on histamine decolorizes the dye indigo-disulphonate. Three modifications of the Kapeller-Adler method were employed: air was used instead of oxygen; the time of incubation was 72 hours; the degree of decolorization was measured by an Evelyn photoelectric colorimeter and expressed in mg. of dye per 1 ml. of serum. It was found that two important factors influenced the decolorization of the dye in this test: (1) nonspecific activity associated with incubation; (2) specific histaminase activity associated with incubation and the presence of histamine in the serum-dye mixture. The test was employed on the sera of 12 nonpregnant women, 40 pregnant women, and nine with pre-eclampsia. The nonspecific activity was the same in all three groups. No evidence of specific histaminase activity was found in the sera of the nonpregnant women. There was definite evidence of histaminase activity in the sera of pregnant women; this activity was low in the first 100 days of pregnancy and high after that time. The sera of patients with pre-eclampsia also showed histaminase activity; no evidence of the inhibition of either nonspecific activity or histaminase activity was found in these cases. Further investigations are needed to determine the function of histaminase in pregnancy; the author suggests that this enzyme may be an important link in the metabolism of histidine during pregnancy. HARVEY B. MATTHEWS.

Necrology

THOMAS WATTS EDEN, M.D., F.R.C.P., F.R.C.O.G., of London, eminent obstetrician, gynecologist, teacher, editor, and author, Honorary Fellow of the American Gynecological Society, died Sept. 22, 1946, at the age of 83 years. Well known as editor of the *Journal of Obstetrics and Gynaecology of the British Empire,* prominently identified with the development of the Chelsea Hospital for Women to an outstanding institution, playing a great part in placing abdominopelvic surgery on a firm foundation, a major in the R.A.M.C. in the first World War, chairman of the committee which developed the scheme for a national midwifery service, and author with Lockyer of a widely used textbook, he was widely recognized as an outstanding member of his specialist group. Upon delivering an address before the American Gynecological Society at its annual meeting in 1920, he was made an honorary member of this body.

Correspondence

Early Diagnosis of Anencephaly

To the Editor:

In the April, 1946, issue of the *Journal* there appeared an article on page 571 by Dr. Catherine W. Blumberg and Dr. George Teplick entitled "Early Clinical and Roentgenologic Diagnosis of Anencephaly." I believe that it is worthy of comment.

The opening sentence reads, "The importance of early diagnosis of fetal monstrosities cannot be too greatly stressed, as it precludes the possibility of unwittingly allowing the patient thus burdened to progress to term." Why? If their management of the case is what they advocate, I should think it would be worth reconsidering. Labor was induced at six months with rupture of the membranes. This was followed by infection of the amniotic sac necessitating the use of penicillin. Then, to add injury to the insult, the cervix was manually dilated from 1 to 2 cm. to 3 to 4 cm. Finally, "after dilatation"(full?), "the macerated anencephalic fetus was extracted with some difficulty."

I cannot see why the life and health of the mother should have been jeopardized for the sake of the premature delivery of a dead baby. Why not let Nature take its own course—and in a much safer manner? I may be wrong, but I think the above treatment was an exceedingly hazardous way of handling a minor obstetric difficulty.

GEORGE SPECK, M.D.

2806 SOUTH RANDOLPH STREET
ARLINGTON, VA.
MAY 13, 1946

Reply by Dr. Blumberg

To the Editor:

Dr. Speck's chief criticism appears to be the management of the case we reported. Apparently it was not noted that, following diagnosis, the patient was referred for further care, since the U. S. Public Health Service Dispensary does not have facilities for prenatal care or delivery. We do not wish to enter upon controversial discussion of obstetric management, but, in defense of the obstetrician who handled this case following our diagnosis, we wish to state that his willingness to submit a summary of the progress and management in order that we might make a complete case report for publication was greatly appreciated and indicates to us that he did not feel a need for justifying his procedure.

A policy to "let Nature take its course" is contrary to the basic need for specialized obstetric training to care for those cases in which Nature's course is abnormal. By letting natural forces dictate management a "minor obstetric difficulty" may become a major one. Two of the patients cited in our report carried their pregnancy three or four weeks beyond term, and one of them was finally delivered by cesarean section.

Applying the principles of good medical practice, we reaffirm that early diagnosis of abnormal conditions, and the prevention of greater complications should be our goal. Opinion may differ as to the advisability of terminating a pregnancy where the fetus is dead, and possibly abnormal, but the final opinion can be rendered in any specific case only by the doctor in attendance.

CATHERINE W. BLUMBERG, M.D.

WASHINGTON, D. C.
AUG. 7, 1946.

Lactobacillus Therapy in Vaginitis Due to Trichomonas

To the Editor:

Everyone who has studied the biology of the vagina knows of the symbiosis between the normal and pathologic flora of microbism there; the relationship between the normal vaginal bacillus and the lactobacillus; and the dependence of these bacilli from glycogen contents of the vaginal epithelium.

Last year, L. Brady and R. D. Reid described in the JOURNAL* a new therapy with lactobacilli in cases of vaginitis due to trichomonas. In so doing they completely overlooked that the same therapy was detected and described about twenty-five years ago and published in the *Zentralblatt für Gynäkologie,* 1920 (Gynaecological University Clinic, Charité, Berlin). What is still more interesting, they used nearly the same methods as the author did long ago. They cultivated the lactobacilli in practically the same way, they gave the same food to these bacilli in order to survive in the vagina the attacks of the pathogenic microbes, they put about one million of these lactobacilli in one tablet—as did the author twenty-five years ago, and they had the same good results in about 70 cases, whereas the author published his results in 250 cases twenty-five years ago.

At that time the living lactobacilli compressed into a tablet of milk sugar were already on the market, called "Bacillosan," and other articles on the same subject were published in medical journals.

As I was very much interested to see my old ideas revived absolutely in the same way with such a striking resemblance in detail—identical twins cannot resemble each other more—I can assure Brady and Reid they will have the same excellent results as I had so long ago.

There is one snag only in this therapy. After years and years the lactobacilli no longer grow in the same strength on the culture medium, and they very often lose the power to grow in a hostile alkaline vaginal medium and to overwhelm the antagonistic trichomonas. They can no longer produce the normal vaginal pH., so that the good results of the beginning become weaker.

Should Brady and Reid repeat the experience in years to come, they will certainly bear in mind the publications of other authors.

ALFRED A. LOESER, M.D.

2 DEVONSHIRE PLACE, LONDON, ENGLAND.

SEPTEMBER 25, 1946.

Reply by Drs. Brady and Reid

To the Editor:

When we first conceived the idea of using lactobacillus therapy in the treatment of vaginitis due to *Trichomonas vaginalis,* we surveyed the literature for previous publications on the subject. Unfortunately, we overlooked the paper published by Dr. Loeser in the *Zentralblatt für Gynäkologie,* 1920, but are glad to have this belated opportunity to call attention to Dr. Loeser's work.

We believe that the measures we are taking will prevent the changes in our cultures that Dr. Loeser refers to in his letter. In the laboratory, we are selecting for the lactobacillus tablets only those strains of lactobacillus which produce consistently large amounts of acid and which are unusually resistant to storage. As a matter of fact, our records in the laboratory clearly show that not only have the number of organisms in the tablets been markedly increased, but also the viability of the organisms has been prolonged during our five years' study of this problem.

LEO BRADY, M.D.
ROGER D. REID, M.D.

BALTIMORE, MD.

OCTOBER 16, 1946.

*Lactobacillus Therapy in Vaginitis Due to Trichomonas, AM. J. OBST. & GYNEC. 50: 509, 1945.

Items

Third American Congress on Obstetrics and Gynecology

St. Louis has been chosen as the meeting place of the Third Annual Congress on Obstetrics and Gynecology, to be held September 8 to 12, 1947. Further particulars will be announced in later issues.

American Board of Obstetrics and Gynecology, Inc.

Examinations

The next written examination (Part I) for all candidates will be held in various cities of the United States and Canada on Friday, Feb. 7, 1947, at 2:00 P.M. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination to be held in Pittsburgh, Pa., June 1 to 7, 1947. All applications must be in the office of the Secretary by Nov. 1, 1946. All candidates, especially those in military service, are requested to keep the Secretary's Office closely informed of changes in address.

Several changes in Board regulations and requirements were put into effect at the last annual meeting of the Board held in Chicago, Illinois, from May 5 to May 11, 1946. Among these is the requirement that case records must now be forwarded to the Secretary's Office from thirty to sixty days after the candidate has received notice of his eligibility for admission to the examinations for certification. Candidates are again notified that they must expect to be examined in both branches of the specialty of obstetrics-gynecology. The Board considers that at least fundamental training and knowledge of both branches of this united specialty are essential, regardless of the fact that a candidate may in his practice major in one or the other branch. At this meeting the Board also ruled that it will not accept the nine months' residency as an academic year toward years of training requirements following the termination of the official period of intern and residency acceleration, April 1, 1946.

Applications for the 1947 examinations cannot be accepted after Nov. 1, 1946. For further information and application blanks address Paul Titus, M.D., Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

PAUL TITUS, M.D.

The following diplomates have been certified and are added to the previously published list: Dr. David A. Conners, 131-07 86 Road, Richman Hill 18, N. Y.; Dr. Joseph Deutsch, 55 E. Washington St., Chicago 2, Ill.; Dr. Robert Wade King, Permanente Foundation Hospital, 280 MacArthur Blvd., Oakland 11, Calif.; Dr. Edwin Vance Lawry, 300 Homer Ave., Palo Alto, Calif.; Dr. Sim Bedford Lovelady, Mayo Clinic, Rochester, Minn.; Dr. William Harvey Mease, 813 Fayette Title & Trust Bldg., Uniontown, Pa.; Dr. Samuel A. Manalan, Morrison Field, West Palm Beach, Fla.; Dr. Edison Lloyd Russell Schram, 870 Wellington St., London, Ontario, Canada; Dr. David Jennings Werner, 4810 N. Newhall Street, Milwaukee, Wis.; Dr. Emanuele Momigliano, 2357 W. Madison Street, Chicago, Ill.

Erratum

In the September issue of the JOURNAL on page 528, under Items, the address of Dr. Herbert Malone Black was stated in error. The correct address is 1401 Taylor Street, Columbia, S. C.